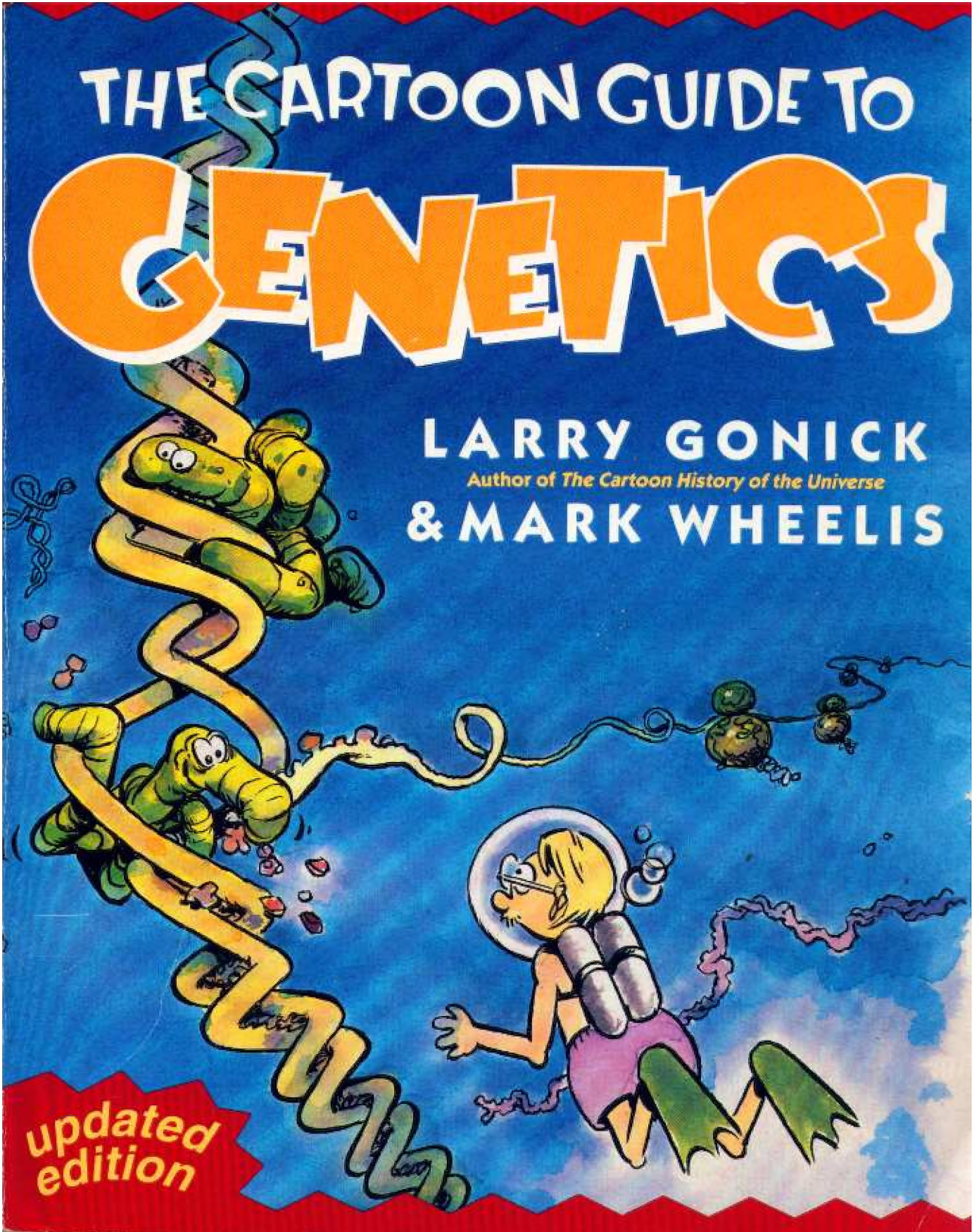


# THE CARTOON GUIDE TO **GENETICS**

LARRY GONICK  
*Author of The Cartoon History of the Universe*  
& MARK WHEELIS

updated  
edition



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FIRST HARPERPERENNIAL edition published 1991

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The Library of Congress has cataloged the previous edition of this book as follows:

Gonick, Larry.

The cartoon guide to genetics.

"CO/416."

Includes index.

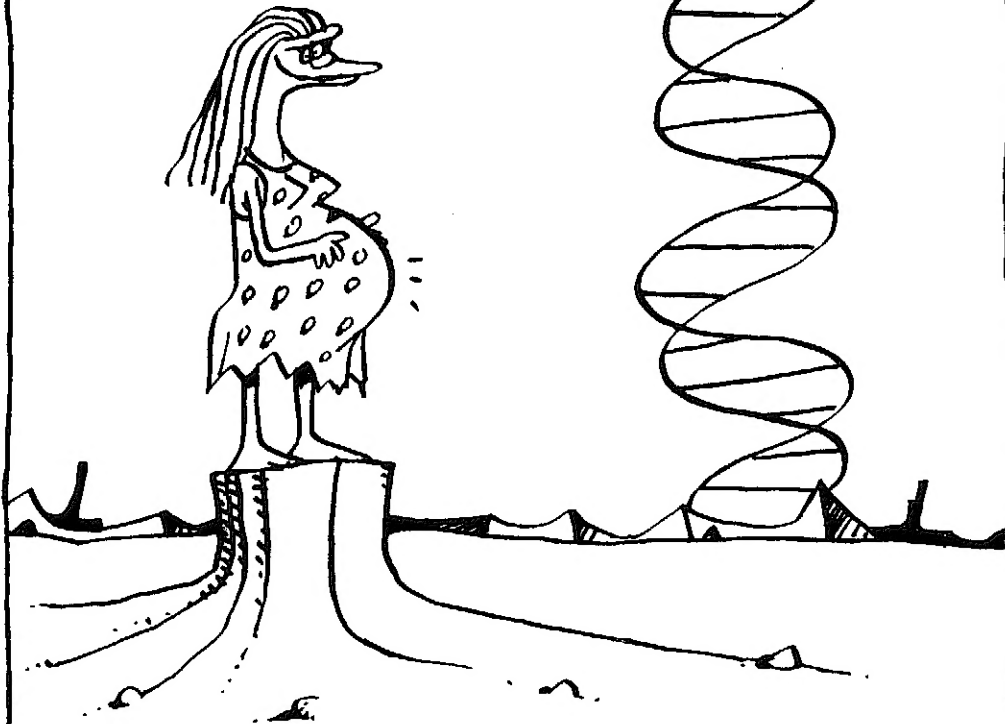
1. Genetics—Caricatures and cartoons. I. Wheelis, Mark. II. Title.  
QH436.G66 1983 575.1'0207 82-48252  
ISBN 0-06-460416-0 (pbk.)

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ISBN 0-06-273099-1 (pbk.)

99 00 01 02 RRD-H 30 29 28 27 26 25 24 23 22

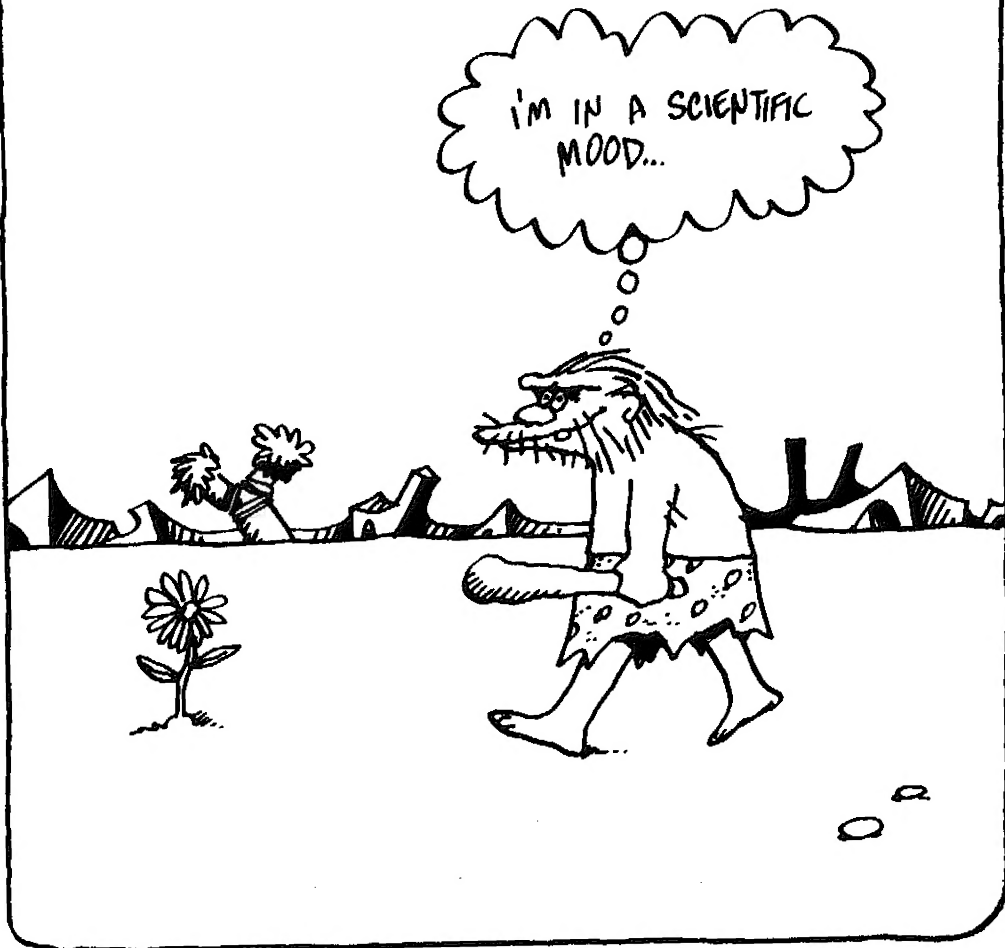
TO REPRODUCTION,  
WITHOUT WHICH  
OUR SUBJECT,  
OUR AUTHORS,  
AND OUR READERS  
WOULD HAVE BEEN  
IMPOSSIBLE...



*grüek\**

# IN ANCIENT TIMES...

OUR ANCESTORS  
HAD A FIRST-HAND  
KNOWLEDGE OF  
NATURE. IN THOSE  
DAYS, EVERYONE WAS  
A BIOLOGIST, AND  
THE WORLD WAS  
A CLASSROOM !!



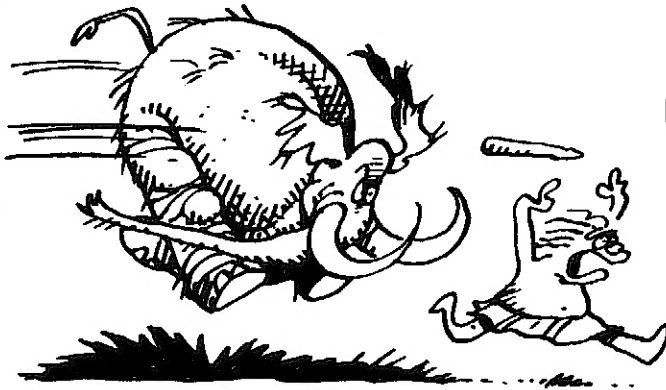


IN THEIR EARLIEST GLIMMERINGS OF THOUGHT, IT'S SAID, PEOPLE MADE NO DISTINCTION BETWEEN LIVING AND NON-LIVING THINGS. EVERYTHING WAS SUPPOSED TO BE ALIVE, A FIT SUBJECT OF "BIOLOGICAL" RESEARCH.

THIS INCLUDED TREES...



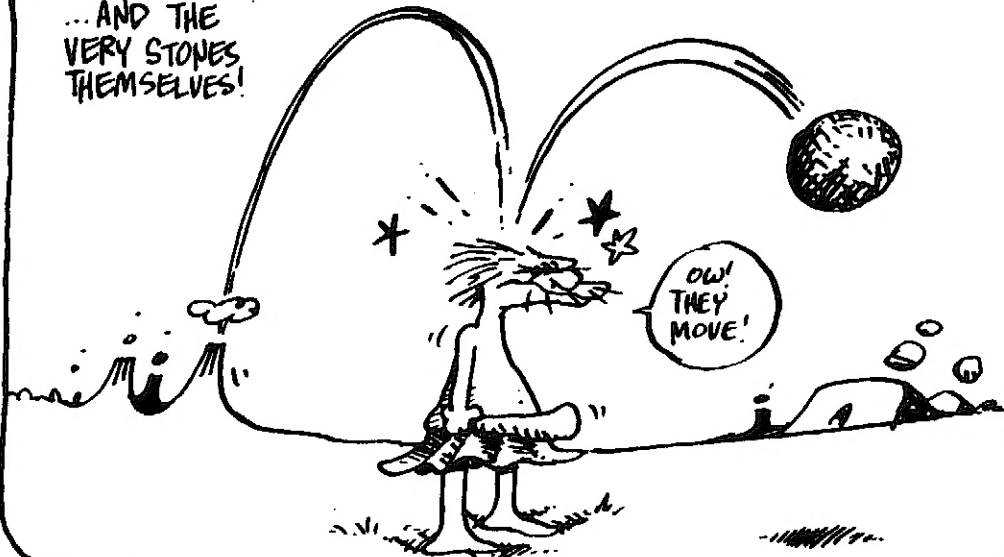
THEY MOVE!



THEY MOVE!

... ANIMALS...

... AND THE VERY STONES THEMSELVES!



OW! THEY MOVE!

IN THE COURSE OF THEIR STUDIES, OUR ANCESTORS MUST HAVE NOTICED AN OBVIOUS FACT: SOME THINGS TENDED TO REPRODUCE THEMSELVES.

PEOPLE  
DID IT...



...MAMMOTHS  
DID IT...



...AND, TO THE  
PRIMITIVE  
MIND, IT MAY  
WELL HAVE  
SEEMED THAT  
EVEN ROCKS  
COULD "GIVE  
BIRTH" TO  
LITTLE PEBBLES!



MANY SCHOLARS BELIEVE THAT PRIMITIVE PEOPLE SAW NO CONNECTION BETWEEN REPRODUCTION AND SEX. THE NINE MONTHS BETWEEN CONCEPTION AND BIRTH WAS SUPPOSEDLY ENOUGH TO STYMIE THE SMARTEST STONE-AGER... AND WHAT DOES SEX HAVE TO DO WITH THE REPRODUCTION OF ROCKS??!!

FOR WEEKS I'VE BEEN WATCHING, AND I DON'T THINK THEY DO IT...



WE MUST ADMIT, THIS THEORY LEAVES US SLIGHTLY SKEPTICAL. IT SEEMS POSSIBLE THAT MEN MIGHT HAVE MISSED THE CONNECTION, BUT COULD WOMEN HAVE OVERLOOKED WHAT WAS HAPPENING TO THEIR OWN BODIES??!

EVER NOTICE ANYTHING FUNNY ABOUT BABIES AND SEX?

YES... YOU CAN'T HAVE ONE WITHOUT THE OTHER...



C'MON... DON'T BE SHY...

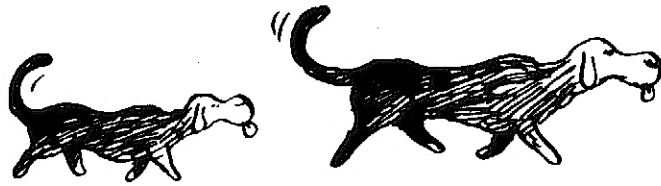
ENLIGHTENMENT CAME,  
ACCORDING TO THIS THEORY,  
WHEN PEOPLE FIRST  
**DOMESTICATED ANIMALS**—  
AND SAW THEIR REPRODUCTIVE  
CYCLE CLOSE-UP AND OFTEN:  
MATING IN ONE SEASON,  
BIRTH IN ANOTHER.



IT MUST HAVE COME  
AS A GREAT SHOCK  
TO DISCOVER THAT  
MEN HAD SOMETHING  
TO DO WITH MAKING  
BABIES... IT'S SAID  
TO HAVE CAUSED  
BIG CHANGES IN  
SOCIETY, SUCH AS  
FATHER'S DAY,  
PATERNITY SUITS,  
MARRIAGE, AND THE  
PATRIARCHY — BUT THIS  
IS A BIOLOGY BOOK,  
AND WE WON'T GO  
INTO ALL THAT...



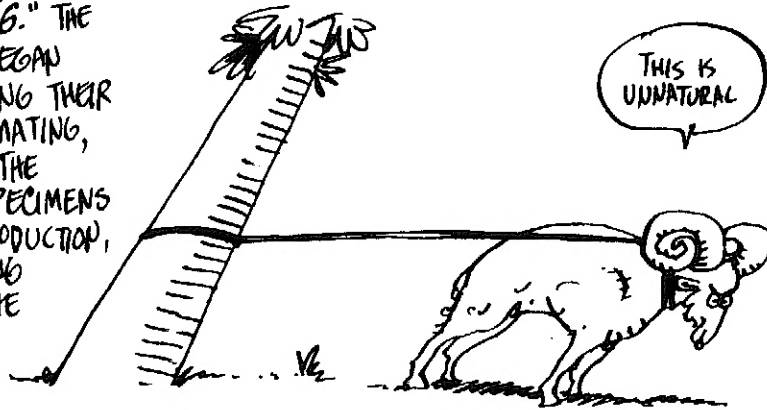
ALONG WITH THIS  
CAME THE NOTION  
THAT LIKE  
BEGETS LIKE—  
THE FIRST REALLY  
GENETIC IDEA..



AND SO BEGAN

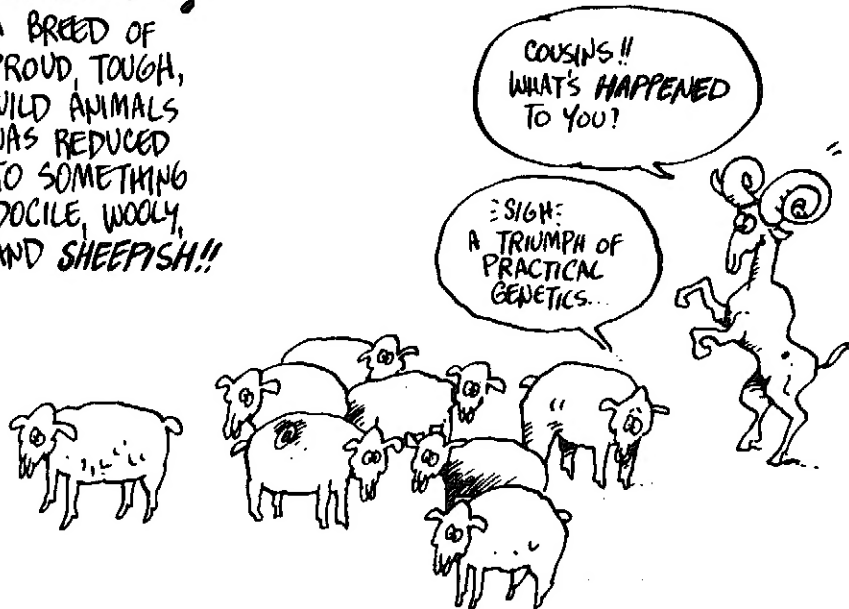
## PRACTICAL GENETICS,

OR "SELECTIVE  
BREEDING." THE  
HERDERS BEGAN  
CONTROLLING THEIR  
ANIMALS' MATING,  
CHOOSING THE  
"BEST" SPECIMENS  
FOR REPRODUCTION,  
AND GETTING  
RID OF THE  
"WORST."



## RESULT ?

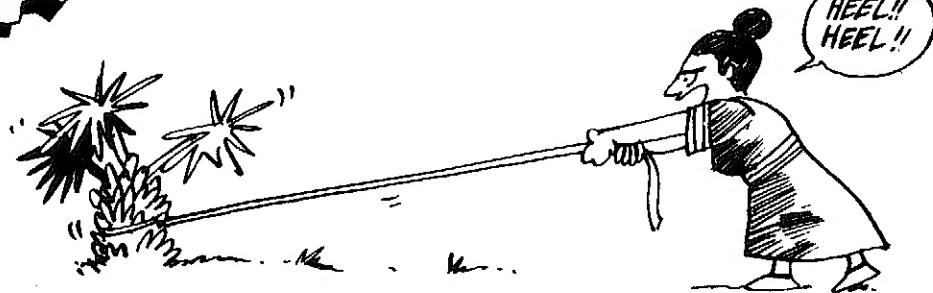
A BREED OF  
PROUD, TOUGH,  
WILD ANIMALS  
WAS REDUCED  
TO SOMETHING  
DOCILE, WOOLLY,  
AND SHEEPISH!!



COUSINS!!  
WHAT'S HAPPENED  
TO YOU?

SIGH:  
A TRIUMPH OF  
PRACTICAL  
GENETICS...

**A** T THE SAME TIME, PEOPLE WERE DOMESTICATING PLANTS:



EARLY FARMERS USED THE SAME METHODS AS THE ANIMAL HERDERS, WEEDING OUT UNDESIRABLE STRAINS AND PLANTING ONLY THE BEST SEEDS.



THIS HAPPENED ALMOST EVERYWHERE IN THE WORLD: SCRAWNY WEEDS AND GRASSES WERE GRADUALLY TURNED INTO RICH, PRODUCTIVE CROPS. RICE, WHEAT, BARLEY, AND DATES IN ASIA; CORN, SQUASH, TOMATOES, POTATOES, AND PEPPERS IN AMERICA; YAMS, PEANUTS, AND GOURDS IN AFRICA — ALL SPECIALLY IMPROVED BY HUMANS !!



PLANTS HAVE SEX, TOO... THEY'RE JUST LESS NOISY ABOUT IT THAN ANIMALS. EARLY ON, PEOPLE NOTICED THE IMPORTANCE OF **POLLINATION**: POLLEN DUST MUST LAND ON A FLOWER BEFORE IT CAN PRODUCE FERTILE SEEDS.



# HOWEVER —

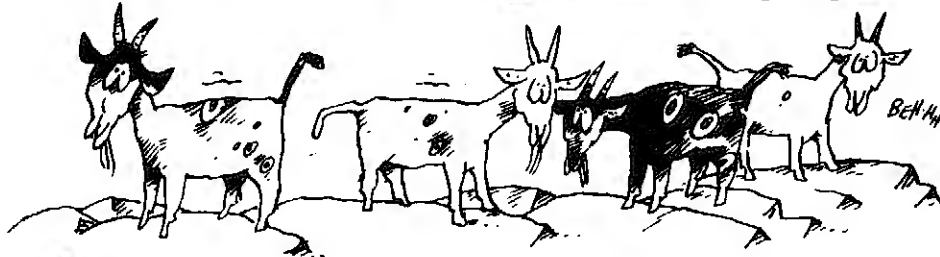
THE EARLY FARMERS REALLY DIDN'T KNOW WHY POLLINATION WORKED — SO THEY ADDED SOME **MAGIC**, JUST TO BE ON THE SAFE SIDE...

THESE ARE ASSYRIAN PRIESTS, POLLINATING A DATE PALM, AROUND 800 B.C.



THIS COMBINATION OF SCIENCE AND MAGIC IS NICELY ILLUSTRATED BY A BIBLE STORY... GENESIS, CHAPTER 30, OR...

## THE CASE OF JACOB'S FLOCK



IN THIS STORY, THE PATRIARCH JACOB AGREES TO TEND THE FLOCK OF HIS FATHER-IN-LAW LABAN. AS PAYMENT, JACOB MAY TAKE ALL THE "SPECKLED AND SPOTTED" ANIMALS FOR HIMSELF, WHILE LABAN KEEPS THE PURE BLACK ONES. THE TWO GROUPS ARE NOT TO INTERBREED.



THE BIBLE DESCRIBES JACOB'S FERTILITY MAGIC CAREFULLY: HE STRIPPED THE BARK FROM WILLOW RODS, AND "MADE THE WHITE APPEAR WHICH WAS IN THE RODS," THEN SET THEM NEAR THE WATERING HOLE.





THE IDEA BEHIND JACOB'S ACTION IS THAT LIKE BEGETS LIKE: BY SHOWING THE WHITE IN THE WILLOW RODS, HE WAS TRYING TO BRING OUT THE WHITE IN LABAN'S BLACK ANIMALS !! THIS IS CALLED SYMPATHETIC MAGIC...



THE POINT, GENETICALLY SPEAKING, IS THIS: IN FACT, THE PURE BLACK ANIMALS **BORE SPECKLED OFFSPRING** —AND SO JACOB'S FLOCK INCREASED! WHY??



WE'LL COME BACK TO THIS LATER!

HERE WE SEE ACCURATE GENETIC OBSERVATION SIDE-BY-SIDE WITH A NEAR TOTAL LACK OF UNDERSTANDING.

LABAN CERTAINLY DIDN'T GET IT!!



SOME OTHER GENETIC ITEMS FROM ANCIENT HISTORY:

THE CHINESE  
DISCOVERED  
"WALTZING" MICE,  
A MUTATION WHICH  
CAUSES THE  
ANIMAL TO STAGGER  
AROUND IN  
CIRCLES.



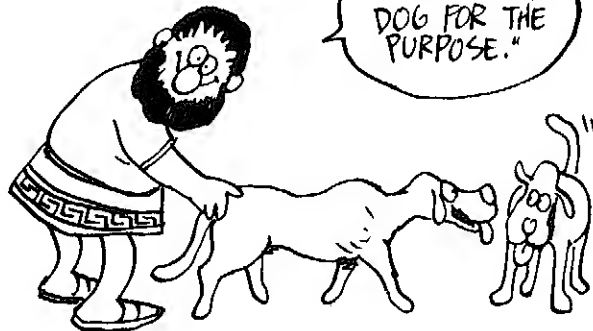
THE HINDUS OBSERVED  
THAT CERTAIN DISEASES  
MAY "RUN IN THE  
FAMILY." MOREOVER,  
THEY CAME TO BELIEVE  
THAT CHILDREN  
INHERIT ALL THEIR  
PARENTS' CHARACTERISTICS.  
"A MAN OF BASE  
DESCENTS CAN NEVER  
ESCAPE HIS ORIGINS,"  
SAID THE LAWS OF  
MANU...

THE  
BASIS  
OF THE  
CASTE  
SYSTEM!

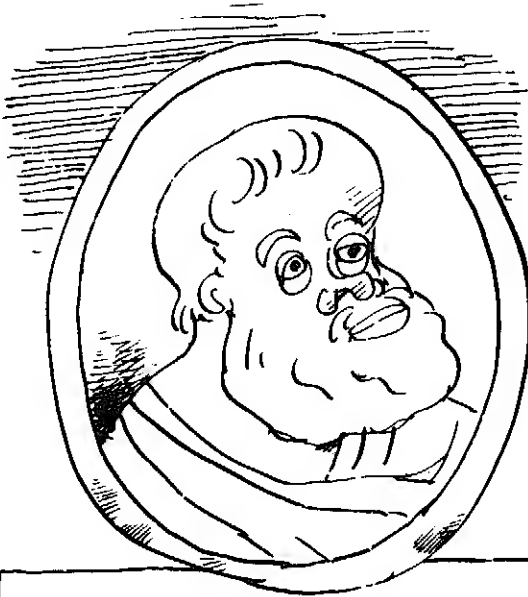


XENOPHON, A GREEK,  
HAD THIS TO SAY  
ABOUT BREEDING  
HOUNDS:

"GET A GOOD  
DOG FOR THE  
PURPOSE."



SEVERAL OTHER GREEKS, THINKING MORE DEEPLY THAN XENOPHON, DEVELOPED THE FIRST REAL THEORIES OF HEREDITY — IN OTHER WORDS, THEY ADDRESSED THE QUESTION: "WHY DO CHILDREN RESEMBLE THEIR PARENTS?"



ACTUALLY, ONE PHILOSOPHER, SOCRATES, WONDERED WHY THEY SOMETIMES DON'T... HE USED TO SAY THAT THE SONS OF GREAT STATESMEN WERE USUALLY LAZY AND GOOD FOR NOTHING... WE SHOULD ALWAYS BEAR THIS IN MIND, THAT NOT EVERY QUALITY IS INHERITED...

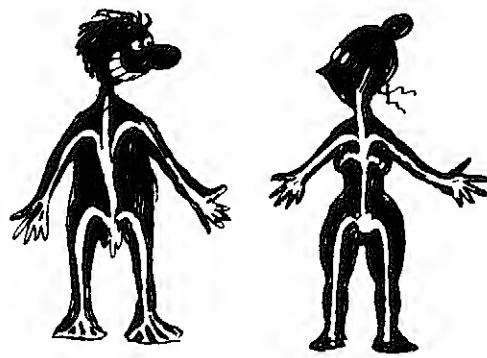
UNFORTUNATELY, BY SUCH UNFLINCHING HONESTY, SOCRATES PROVOKED THE ATHENIANS TO PUT HIM TO DEATH...



THE MOST COHERENT  
GREEK THEORY OF  
HEREDITY WAS THAT  
OF THE FAMOUS DOCTOR  
HIPPOCRATES.



HIPPOCRATES  
RECOGNIZED THAT  
THE MALE CONTRIBUTION  
TO A CHILD'S  
HEREDITY IS CARRIED  
IN THE SEMEN.  
BY ANALOGY, HE  
ASSUMED THERE WAS  
A SIMILAR FLUID IN  
WOMEN.

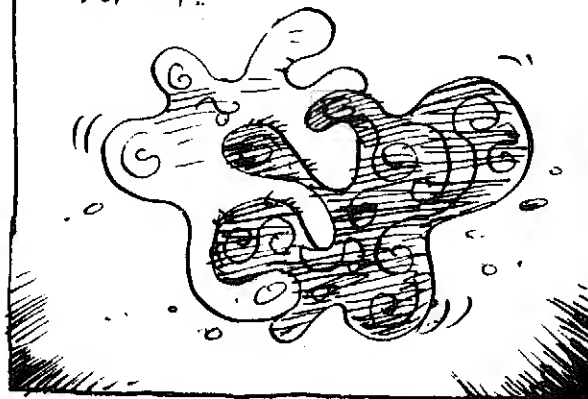


THESE FLUIDS, HE REASONED,  
WERE MADE THROUGHOUT THE  
BODY, AND THEN COLLECTED IN THE  
REPRODUCTIVE ORGANS.



THE SEMEN  
FROM THE FINGERS  
HAD THE MATERIAL  
TO MAKE MORE  
FINGERS; THAT  
FROM THE HAIR  
MADE HAIR, ETC  
ETC ETC...

AT CONCEPTION, A SORT OF  
BATTLE OF THE FLUIDS TOOK PLACE,  
AND WHETHER THE CHILD'S HANDS  
WERE MORE LIKE MOM'S OR DAD'S  
DEPENDS ON WHOSE FINGER-SEMEN  
WON OUT!!





UNFORTUNATELY, THE GREEK WHOSE IDEAS MOST INFLUENCED LATER GENERATIONS WAS NOT HIPPOCRATES, BUT **ARISTOTLE**. WHEN IT CAME TO SCIENCE, ARISTOTLE NEVER LET HIS IGNORANCE STAND IN THE WAY OF HIS THEORIES!!



BIOLOGY?  
I CAN DO IT  
WITH MY  
EYES CLOSED!

ARISTOTLE — CALLED "THE PERIPATETIK" BECAUSE HE PACED WHILE HE LECTURED — BELIEVED THAT ALL INHERITANCE CAME FROM THE **FATHER**... THE MALE SEMEN, HE SAID, DETERMINED THE BABY'S FORM, WHILE THE MOTHER MERELY PROVIDED THE MATERIAL FROM WHICH THE BABY WAS MADE...

BUT, ARI —  
THEN, WHERE DO  
**GIRLS** COME  
FROM?



YES, THERE WAS NO GETTING AROUND IT... THIS SEEMED TO IMPLY THAT ALL CHILDREN OUGHT TO BE BOYS... WHO KNOWS? MAYBE THIS REVEALED SOME SUBCONSCIOUS WISH OF ARISTOTLE'S... THE ANCIENT GREEKS DID VALUE BOYS MORE HIGHLY THAN GIRLS.



IN MY VERSION OF THE IDEAL STATE, ALL PHILOSOPHERS WOULD BE REQUIRED TO GET PREGNANT, AT LEAST ONCE...

BUT THE PHILOSOPHER COULD HARDLY IGNORE THE EXISTENCE OF FEMALE BABIES. HE PATCHED UP HIS THEORY BY DECLARING THEY WERE CAUSED BY "INTERFERENCE" FROM THE MOTHER'S BLOOD.



AND NOW, ON TO PHYSICS...

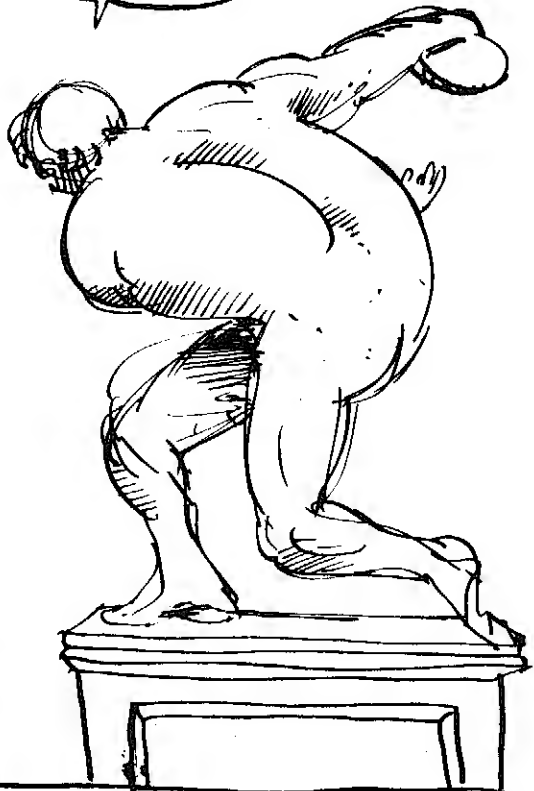
WHOSE FLUIDS  
MADE MY SPECKLES?



A FINE THEORY ... EXCEPT  
THAT IT DOESN'T ACCOUNT  
FOR CHILDREN WHO DIFFER  
FROM **BOTH** PARENTS!  
BROWN-EYED PEOPLE OFTEN  
HAVE BLUE-EYED BABIES,  
AND DON'T FORGET JACOB'S  
SPECKLED GOATS.

ONE PHILOSOPHER,  
EMPEDOCLES,  
THOUGHT THIS  
MIGHT RESULT  
FROM THE  
MOTHER'S  
GAZING  
LONGINGLY  
AT STATUES  
DURING  
PREGNANCY.

WHAT'S WRONG,  
LADY? LOST  
YOUR MARBLES?



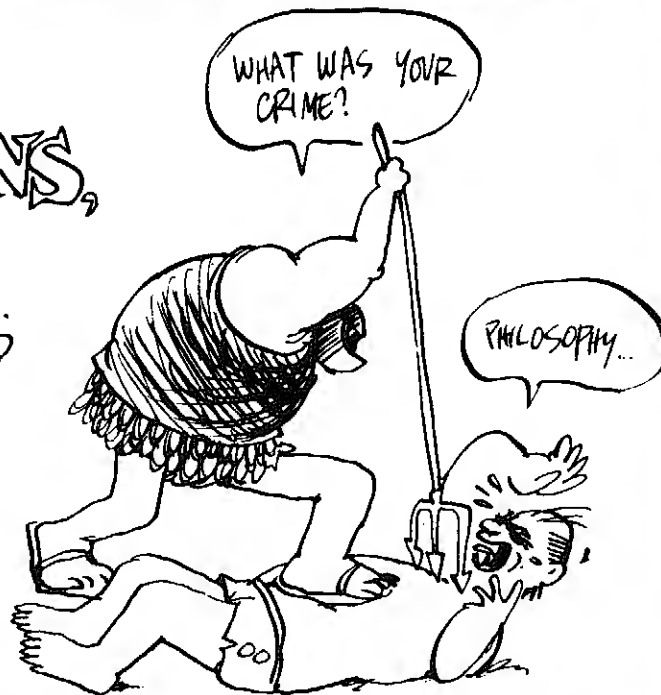
GREEK CIVILIZATION MAY HAVE PERISHED, BUT...

# SCIENCE MARCHES ON!

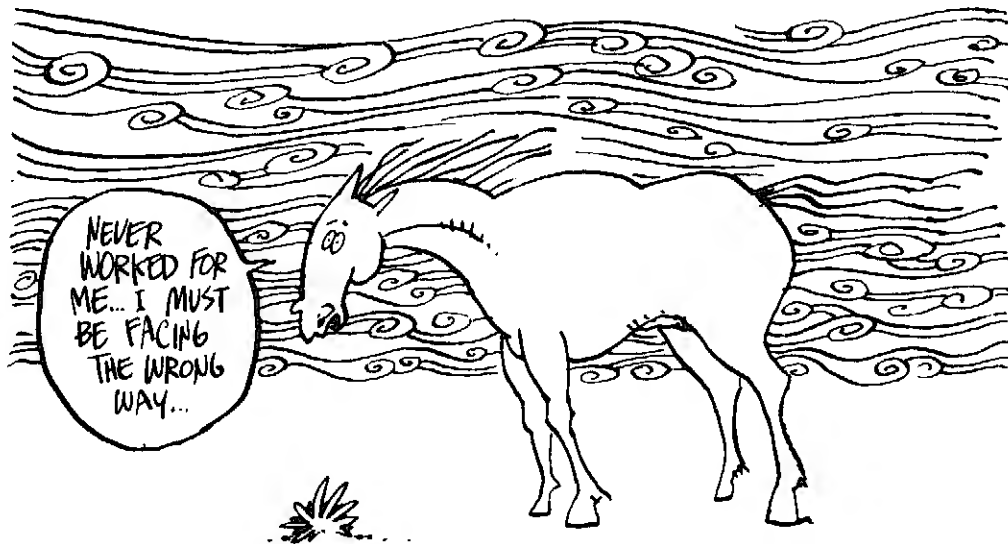




THE GREEK  
MANTLE PASSED  
TO THE  
**ROMANS,**  
WHO HAD  
LITTLE TASTE  
FOR PHILOSOPHY...  
THEY PREFERRED  
THE TECHNOLOGY  
OF DEATH  
TO THE  
SCIENCE OF  
LIFE.



THE ONLY GENETIC IDEA THEY ADDED WAS THAT MARES  
COULD BE FERTILIZED BY THE WIND...

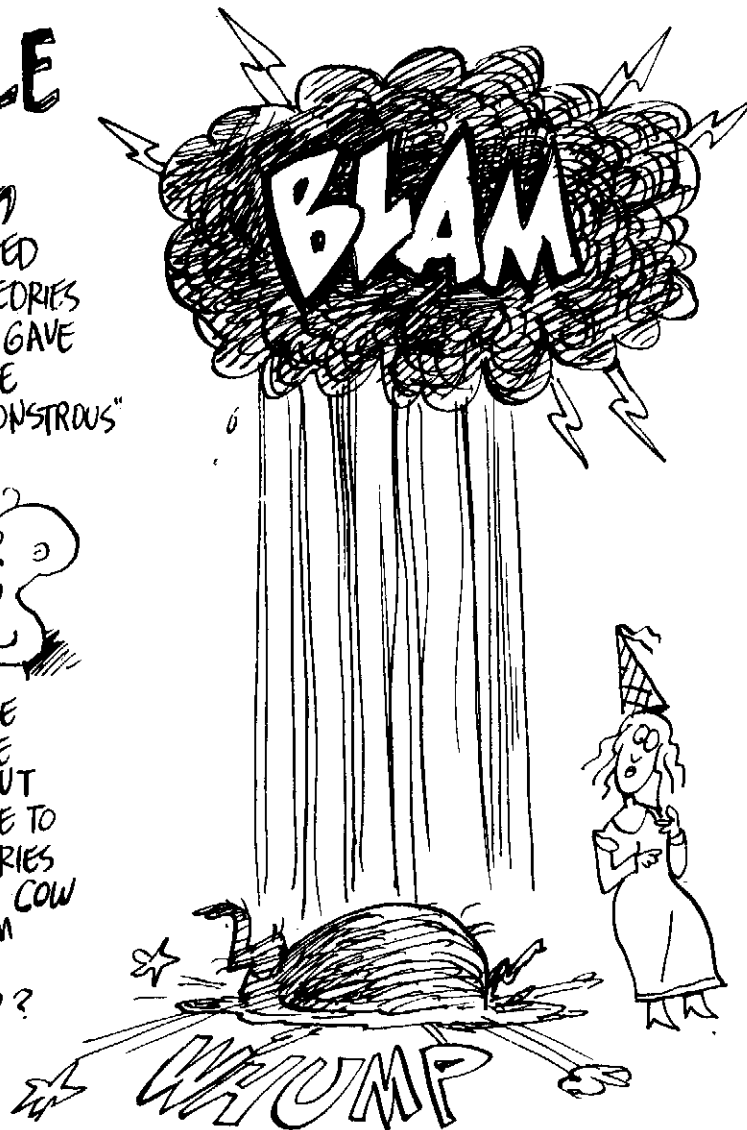


# IN THE MIDDLE AGES,

SCIENCE FADED  
FURTHER... THEORIES  
OF HEREDITY GAVE  
WAY TO MERE  
LISTS OF "MONSTROUS"  
BIRTHS...



SOME OF THESE  
MAY WELL BE  
GENUINE — BUT  
WHAT ARE WE TO  
MAKE OF STORIES  
LIKE HALF A COW  
FALLING FROM  
HEAVEN IN A  
THUNDERCLAP?



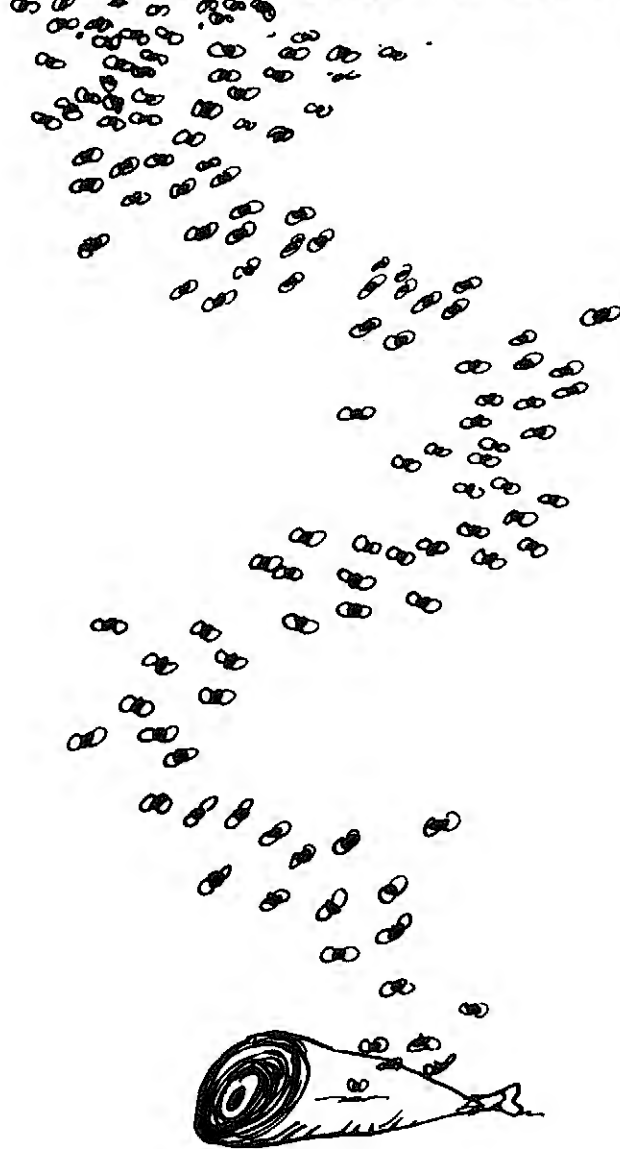
THERE'S ALWAYS THE  
CHANCE IT WAS JUST  
A TALL TALE... OR  
SOMEONE'S IDEA OF  
A JOKE...



YES... REMINDS  
ME OF THE ONE  
ABOUT THE  
PRIORRESS, THE  
ARCHDEACON,  
AND THE  
TWO-HEADED  
SWINE...

ONE MEDIEVAL IDEA ESPECIALLY  
IMPEDED UNDERSTANDING. IT WAS CALLED:

# SPONTANEOUS GENERATION



IT'S  
COMMON  
SENSE!



ORIGINATING  
WITH THE GREEKS,  
THIS WAS THE  
BELIEF THAT  
LIVING  
ORGANISMS  
COULD ARISE  
("SPONTANEOUSLY")  
FROM NON-  
LIVING MATTER.

MAMA!



MAGGOTS WERE  
SUPPOSED TO COME  
FROM DECAYING  
MEAT... HORSEHAIR  
TURNED INTO  
WORMS... AND  
FROGS, MICE, AND  
BUGS WERE  
NOTHING BUT SLIME  
COME TO LIFE!!

YOU CAN'T  
TELL ME  
OLD  
ARMOR  
DOESN'T  
BREED  
FLEAS!



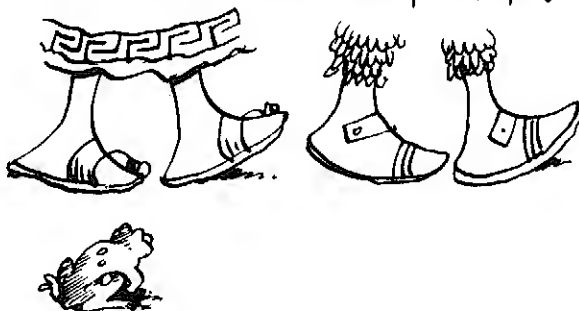
IT'S NOT HARD TO  
IMAGINE WHY  
SPONTANEOUS  
GENERATION SEEMED  
PLAUSIBLE:  
IN A WORLD  
WHERE SLIME  
WAS COMMON,  
ONE SAW IT  
HAPPEN  
EVERY DAY!

YOU SEE HOW BELIEF IN SPONTANEOUS  
GENERATION CONFLICTS WITH  
"GENETIC" THINKING? IF A FROG  
COMES FROM SLIME, IT  
DOESN'T MAKE MUCH  
SENSE TO TALK ABOUT  
INHERITED QUALITIES,  
DOES IT??

NOT MUCH  
FAMILY RESEM-  
BLANCE, IS  
THERE?



BUT - AS WE MENTIONED, SCIENCE MARCHES ON...



AND IN THE 17<sup>TH</sup>  
CENTURY, A SIMPLE  
EXPERIMENT  
SUCCESSFULLY  
CHALLENGED  
SPONTANEOUS  
GENERATION..

THE ELEGANT  
DEMONSTRATION  
WAS PERFORMED  
BY THE  
ITALIAN  
FRANCESCO  
REDI...

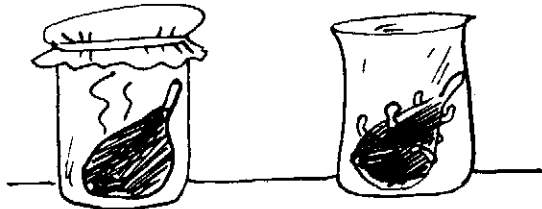


WHEN  
THE TIME  
IS RIGHT,  
THE MAP  
MUST  
BE  
REDI!

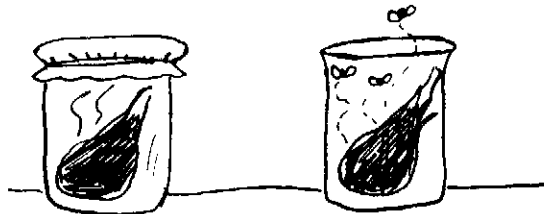
REDI PLACED PIECES OF FRESH  
MEAT IN JARS... SOME OF THE JARS  
HE CAPPED TIGHTLY WITH CHEESE-  
CLOTH, WHILE LEAVING THE REST  
OPEN TO THE FLIES...



AFTER SOME TIME HAD PASSED,  
REDI FOUND MAGGOTS ONLY IN  
THE OPEN JARS.

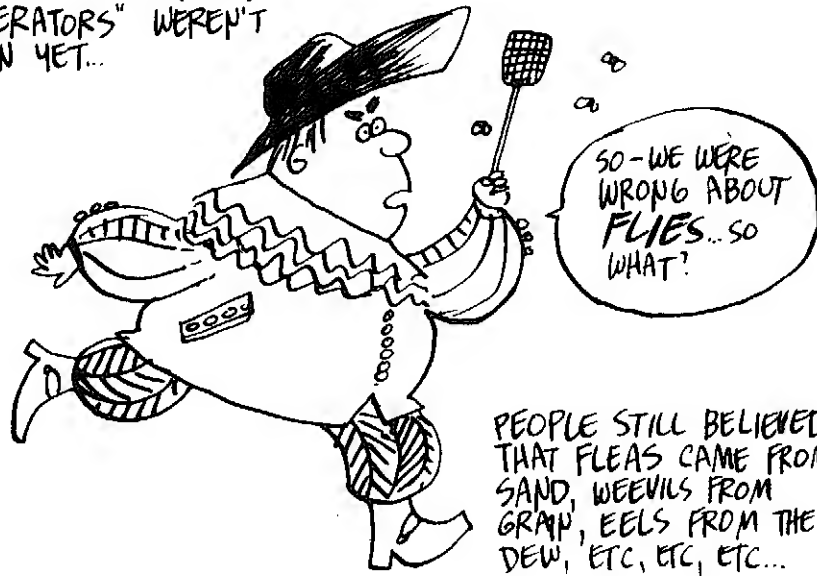


THE MAGGOTS GREW, STIFFENED INTO  
COCOONS, AND FINALLY EMERGED AS  
FULLY FORMED FLIES!



THUS, REDI HAD SHOWN THAT  
MAGGOTS COME FROM FLIES, AND  
FLIES COME FROM MAGGOTS.  
NOTHING VISIBLE HAD BEEN  
"SPONTANEOUSLY GENERATED" FROM  
THE ROTTING MEAT!!

BUT THE "SPONTANEOUS  
GENERATORS" WEREN'T  
DOWN YET...



\*\*\*\*\*

FLEAS, EELS, AND  
WEEVILS, IN TURN,  
WERE DISPOSED OF  
BY ANTON VAN  
LEEUVENHOEK  
("LAY-VEN-HOOK"), AN  
AMATEUR DUTCH  
SCIENTIST AND THE  
FIRST TO MAKE  
SYSTEMATIC USE  
OF THE  
MICROSCOPE.





USING HIS SIMPLE  
INSTRUMENT — JUST  
AN EXCELLENT EYEPiece  
REALLY — LEEUWENHOEK  
FOLLOWED THE LIFE  
HISTORIES OF VARIOUS  
SMALL CREATURES.  
HIS TREATISE ON  
THE FLEA IS A  
CLASSIC!!

"THIS MINUTE AND  
DESPISED CREATURE,"  
[HE WROTE] "IS ENDOWED  
WITH AS GREAT A  
PERFECTION IN ITS KIND  
AS ANY LARGE ANIMAL."



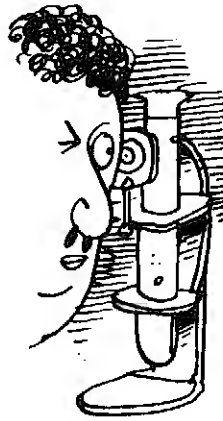
HE DISCOVERED THAT FLEAS, LIKE FISH, DOGS, AND  
HUMANS, WERE **SEXUAL BEINGS!**

MARK MY WORDS:  
FREE INQUIRY CAN  
ONLY LEAD TO  
FREE LOVE...



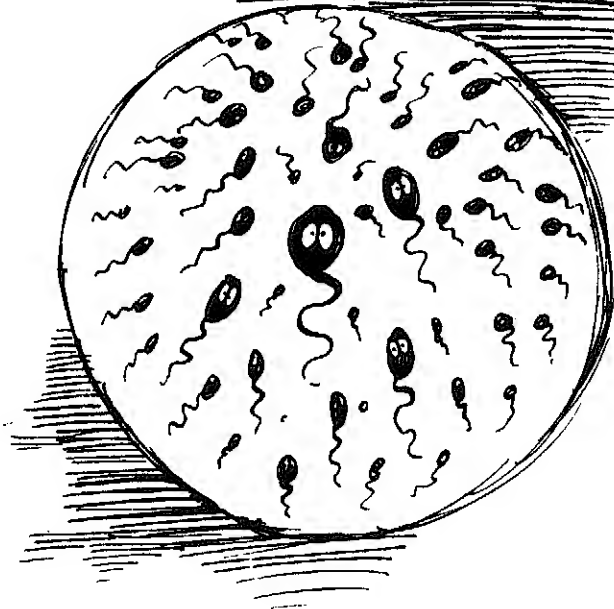
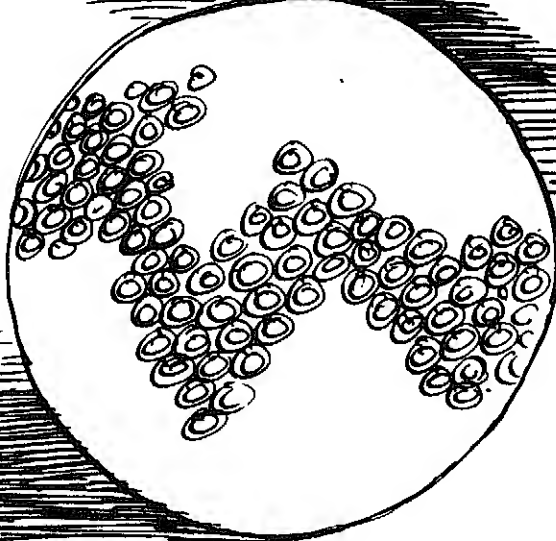
YES... LEEUWENHOEK HAS  
ALREADY CORRUPTED  
THE MORALS OF  
THE FLEA...



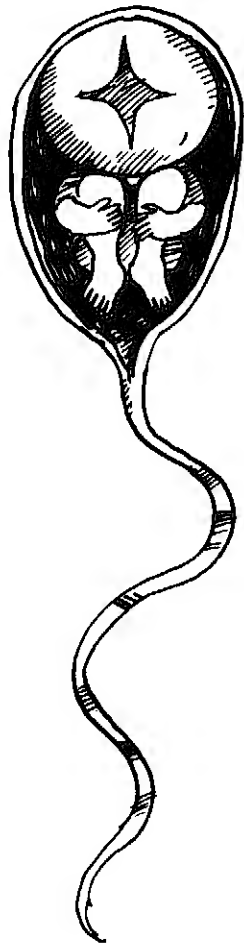


THE DUTCH SCIENTIST  
MADE TWO MORE  
GREAT DISCOVERIES:

HE WAS THE FIRST  
TO SEE  
**BACTERIA**,  
THE ULTRA-SMALL  
ORGANISMS WHICH  
HAVE BECOME  
SO IMPORTANT IN  
MODERN GENETICS  
RESEARCH.

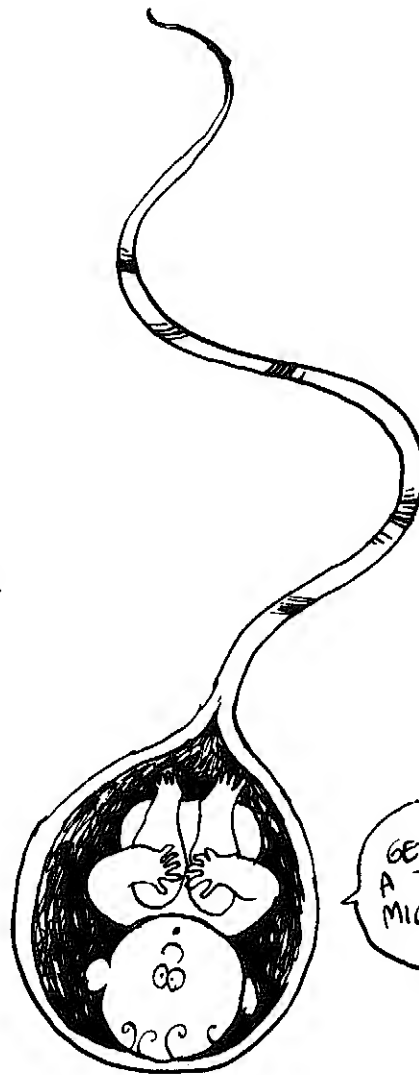


AND HE DISCOVERED  
THE EXISTENCE OF  
**SPERM CELLS**.  
EXAMINING SEMEN,  
LEEUVENHOEK SAW  
MILLIONS OF THESE  
TINY "WORMS."



ONE MIGHT SAY THAT THIS  
DISCOVERY OPENED A WHOLE  
CAN OF WORMS...OR THAT  
IT SPAWNED WRONG IDEAS...  
FOR INSTANCE, LEEUWENHOEK  
HIMSELF BELIEVED EACH SPERM  
CELL CONTAINED A COMPLETE  
NEW ORGANISM IN  
MINIATURE.

THE OBVIOUS PROBLEM WAS:  
IF THIS "PRE-FORMED"  
ORGANISM WAS A BOY, IT  
MUST ALREADY HAVE TINY  
TESTICLES, WHICH WOULD  
CONTAIN MINIATURE  
SPERM, WHICH WOULD  
EACH HAVE EVEN TINIER  
PREFORMED ORGANISMS...  
AD INFINITUM ET  
ABSURDUM !!!



GET ME  
A TINY  
MICROSCOPE!!

# EX OVO OMNIA

(AS LONG AS WE'RE TALKING LATIN!)

WHILE LEEUWENHOEK SPECULATED ABOUT SPERM, OTHER SCIENTISTS WERE LOOKING INTO THE FEMALE ROLE IN REPRODUCTION...



WILLIAM HARVEY (1578-1657) STUDIED THE DEVELOPMENT OF THE CHICK EMBRYO AND CONVINCED HIMSELF THAT ALL ANIMALS MUST COME FROM EGGS. "EX OVO OMNIA," HE SAID: "OUT OF EGG, ALL."

HARVEY BEGAN THE HUNT FOR THE MAMMALIAN EGG.

HE PERSUADED THE KING TO LET HIM LOOK FOR MAMMAL EGGS IN THE ROYAL DEER PARK... DOZENS OF DISSECTED DEER LATER, HARVEY HAD TO ADMIT FAILURE.

SIGH-  
GUESS I' LAID  
AN EGG...



EX OVO  
OMELET!

FOR 200 YEARS THE HUNT WENT ON... AND STILL NO ONE COULD LOCATE THE ELUSIVE EGG.

IT'S NOT HARD TO SEE WHY NOT... NOT ONLY IS THE MAMMALIAN EGG MICROSCOPIC, IT'S ALSO FAIRLY RARE...



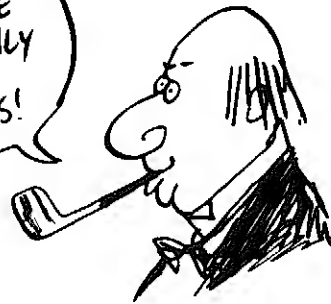
MAMMALS "LAY"  
VERY FEW EGGS:  
A HUMAN FEMALE  
PRODUCES ONLY  
ONE A MONTH,  
IN CONTRAST  
TO THE MALE  
AND HIS  
TENS OF MILLIONS  
OF SPERM  
CELLS.



WASTREL!

BUT THE SEARCH  
WENT ON...THERE WERE  
SOLID REASONS FOR  
BELIEVING MAMMALS  
HAD EGGS: WE HAVE  
OVARIES AND OVIDUCTS...  
IT WOULD BE PRETTY  
SILLY NOT TO HAVE  
EGGS, TOO...

YES,  
PEOPLE ARE  
JUST HIGHLY  
EVOLVED  
CHICKENS!



IN FACT, SCIENTISTS GREW SO SURE EGGS WERE THERE, THAT  
WHEN ONE WAS FINALLY SEEN — A DOG'S EGG, IN 1827 —  
IT CAME AS MORE OF A RELIEF THAN A SURPRISE !!

HEY! DOGS  
GOT EGGS!

YOO-HOO!

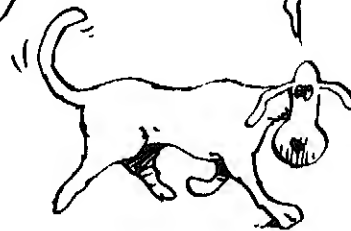
OVER  
HERE!

I SAW  
IT!

HEY!

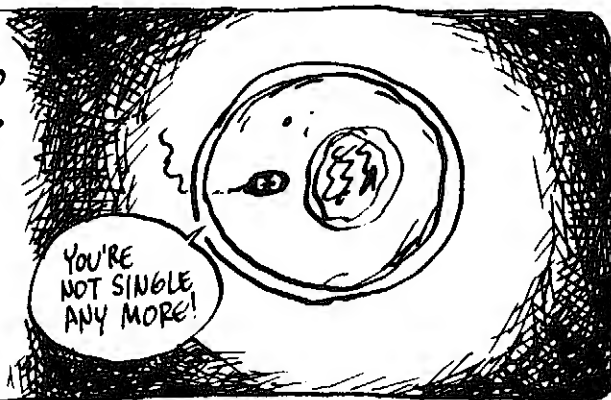


SIGH:  
IT'S ABOUT  
TIME...



THE ONLY REMAINING  
RIDDLE WAS ANSWERED  
WHEN OSCAR HERTWIG  
OBSERVED THAT  
FERTILIZATION  
WAS THE UNION OF  
A SINGLE SPERM  
WITH A SINGLE EGG.

YOU'RE  
NOT SINGLE  
ANY MORE!



# MEANWHILE,

SOME PROGRESS  
HAD BEEN  
MADE IN THE  
QUESTION OF  
PLANT SEX.

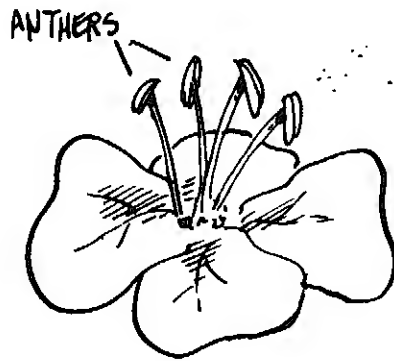


By 1700, THE  
SEXUAL NATURE OF  
PLANTS HAD BEEN  
LARGELY RESOLVED  
BY CAMERARIUS  
(1665-1721), WHOSE  
NAME EVEN SOUNDS  
LIKE A PLANT...

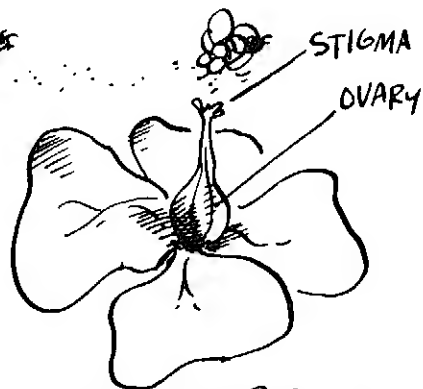
CAMERARIUS SHOWED THAT FLOWERS BORE SEX ORGANS  
QUITE LIKE THOSE OF ANIMALS.

AND THEY STICK  
THEM RIGHT IN  
THE AIR...  
SHAMEFUL!



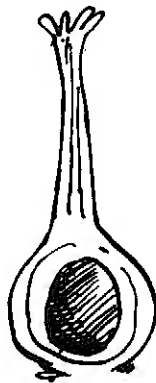


THE MALE PARTS, **ANTHERS**,  
CONTAIN **POLLEN**, WHICH  
IS LIKE **SPERM** IN ANIMALS.

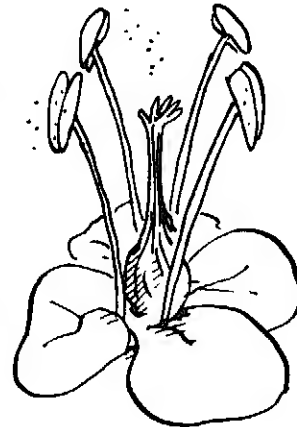


THE FEMALE PART IS  
THE **STIGMA**, TO WHICH  
THE **POLLEN** ATTACHES.

THE **POLLEN**  
(OR PART OF  
IT) THEN  
PENETRATES  
TO THE  
**OVARY**,  
CAUSING  
**SEEDS**  
TO DEVELOP

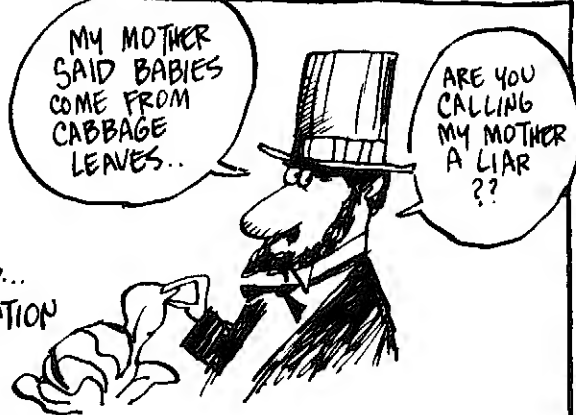


JUST TO  
COMPLICATE  
MATTERS,  
MANY FLOWERS  
HAVE BOTH  
MALE AND  
FEMALE  
ORGANS —  
AND SO THEY  
CAN FERTILIZE  
THEMSELVES.



**SO**

BY THE  
EARLY 1800'S, BOTH  
PLANTS AND ANIMALS  
WERE KNOWN TO BE  
SEXUAL... THE MALE  
CONTRIBUTED **POLLEN** OR  
**SPERM**; THE FEMALE **EGGS**...  
AND SPONTANEOUS GENERATION  
WAS ON ITS LAST  
LEGS — ALMOST...



MY MOTHER  
SAID BABIES  
COME FROM  
CABBAGE  
LEAVES...

ARE YOU  
CALLING  
MY MOTHER  
A LIAR  
??



# TO BREED OR NOT TO BREED?



WITH ALL THIS TALK ABOUT SCIENTISTS, LET US NOT FORGET THE PRACTICAL GENETICISTS -

NAMELY, THE FARMERS AND STOCKBREEDERS WHO DID ALL THE DIRTY WORK OUT IN THE FIELDS.

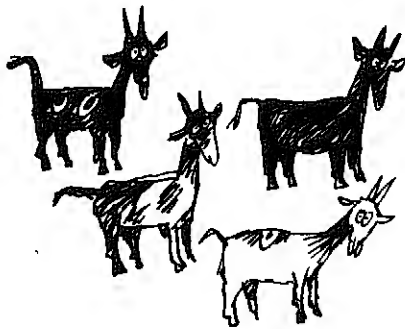


FOR THEM, THE EARLY 19<sup>TH</sup> CENTURY WAS ALSO A TIME OF GREAT PROGRESS WHEN PRACTICAL QUESTIONS OF FARMING WOULD LEAD, MORE OR LESS DIRECTLY, TO THE DISCOVERY OF THE GENE.

LET'S SEE WHAT THEY ALREADY KNEW FROM EXPERIENCE:

1.

SOME **STABLE VARIETIES** NEARLY ALWAYS BREED TRUE, THEIR OFFSPRING HAVING THE SAME CHARACTERISTICS AS THEIR PARENTS. SOME COMMON EXAMPLES ARE MACKINTOSH APPLES, ARABIAN HORSES, LABRADOR RETRIEVERS, PEOPLE WITH BLUE EYES, ETC ETC ETC...



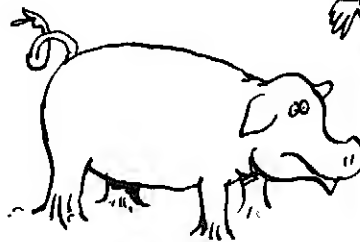
ON THE OTHER HAND, SOME BREEDING GROUPS SHOW GREAT VARIATION. JACOB'S FLOCK IS AN EXAMPLE OF VARIABLE COLOR. PEOPLE WITH BROWN EYES CAN HAVE BLUE-EYED CHILDREN.

2.

IT IS SOMETIMES POSSIBLE TO MATE PARENTS FROM TWO DIFFERENT VARIETIES TO FORM **HYBRIDS**.

FOR EXAMPLE, A MULE IS HALF HORSE AND HALF DONKEY. OF COURSE, NOT ALL HYBRIDS ARE POSSIBLE !!!

IMPOSSIBLE HYBRIDS:



PIG/TREE



HUMAN/STRAWBERRY

HYBRIDS ARE DIFFICULT TO PREDICT... THEY MAY SEEM VIRTUALLY IDENTICAL TO ONE PARENT, OR THEY MAY COMBINE FEATURES OF BOTH — AND WHEN HYBRIDS BREED WITH HYBRIDS, THE RESULT IS VARIATION IN THE EXTREME!!

HARD TO BELIEVE YOU'RE MY BROTHER!



**3.** ALL VARIETIES, EVEN STABLE ONES, OCCASIONALLY PRODUCE "SPORTS" — OFFSPRING DIFFERENT FROM EITHER PARENT. THESE ARE OFTEN GROSSLY DEFECTIVE "MONSTROSITIES"...

OUR CHILD IS A MESS!

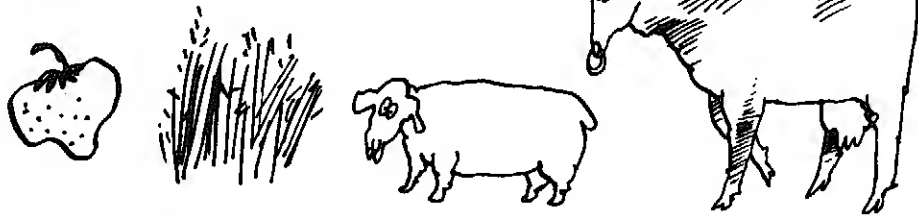


A DACHSHEEP!



BUT SOMETIMES THE SPORT DIFFERS ONLY SLIGHTLY, LIKE THE STUBBY-LEGGED SHEEP WHICH APPEARED AROUND 1800.

BY CROSSING THESE SPORTS BACK WITH NORMAL TYPES, 19TH-CENTURY FARMERS HAD MANAGED TO CREATE SEVERAL NEW STABLE VARIETIES. THERE WERE NEW TYPES OF WHEAT, PEAS, AND STRAWBERRIES, HORNLESS CATTLE, AND STUBBY-LEGGED SHEEP.



BUT IT WAS STILL A MATTER OF TRIAL AND ERROR... IT DIDN'T ALWAYS WORK... AND SO PEOPLE BEGAN TO WONDER IF THERE MIGHTN'T BE A SCIENTIFIC WAY OF SELECTING ADVANTAGEOUS TRAITS TO CREATE NEW VARIETIES.

IF WE COULD BREED A SIX-LEGGED HORSE, WE'D CLEAN UP IN GLUE!

AND A THREE-LEGGED HUMAN COULD PUT HIS FOOT IN HIS MOUTH AND STILL WALK!



# HOWEVER,

DESPITE A GOOD DEAL  
OF WORK, NO TRULY GENERAL  
LAWS OF INHERITANCE WERE  
DISCOVERED.

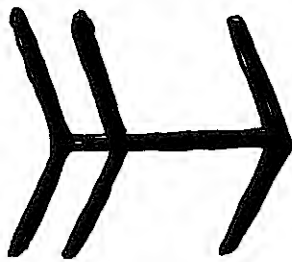
SOME INVESTIGATORS CONFUSED THEMSELVES BY CROSSING  
BREEDS THAT DIFFERED IN TOO MANY CHARACTERISTICS...



OTHERS FAILED  
TO KEEP A  
CAREFUL COUNT  
OF THE NUMBER  
OF VARIETIES  
PRODUCED  
FROM EACH  
CROSS.



NO# FLEAS  
ARE HARD TO  
KEEP TRACK  
OF!



INDEED, THE PROBLEM SEEMED  
HOPELESS... GRADUALLY, SCIENTISTS  
GAVE UP TRYING AND TURNED TO  
EASIER PROBLEMS... AND THAT IS WHY,  
WHEN THE LAWS OF INHERITANCE WERE  
FINALLY FIGURED OUT, THE  
DISCOVERY WAS IGNORED FOR  
THIRTY YEARS...

# MONK FINDS GENE; WORLD YAWNS!



FIFTY YEARS OF RESEARCH HAD FAILED TO FIND ANY PRECISE LAW OF INHERITANCE. OBVIOUSLY, DISCOVERING THE RIGHT FORMULA, IF POSSIBLE, WAS A JOB REQUIRING SUPERHUMAN PATIENCE, UNLIMITED TIME, AND, AS IT HAPPENED, A MIRACLE OF LUCK.

NO WONDER IT HAPPENED IN A MONASTERY...

## GREGOR MENDEL

(1822-1884) WAS AN AUGUSTINIAN MONK FROM BRÜNN, AUSTRIA. IN HIS SPARE TIME, MENDEL BRED PEA PLANTS IN THE MONASTERY GARDENS.



BUT MENDEL WAS NOT JUST AN AMATEUR GARDENER, BUT A **SCIENTIST** WHO STUDIED HIS PEA PLANTS MOST CAREFULLY — HE CALLED THEM HIS "CHILDREN."

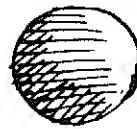


WHAT KIND OF DAD DOES EXPERIMENTS ON HIS KIDS?

CHOOSING PEAS WAS THE MIRACLE OF LUCK: THEY ARE PERFECTLY SUITED TO GENETIC RESEARCH, WITH A NUMBER OF STABLE VARIETIES WHICH MAY FORM HYBRIDS:



THERE WAS A TALL VARIETY AND A SHORT ONE...



ONE TYPE MADE SMOOTH, ROUND PEAS, WHILE ANOTHER'S WERE LUMPY AND WRINKLED...



SOME PODS WERE PLUMP, WHILE OTHERS WERE PINCHED...

THERE WERE GREEN PEAS AND YELLOW; GREY SEED COATS AND WHITE; WHITE FLOWERS AND PURPLE. THERE WERE DIFFERENCES IN THE COLOR OF THE UNRIPE PODS, THE COLOR OF SEED ALBUMIN, AND THE POSITION OF THE FLOWERS.

EVERY PEA FLOWER  
HAS BOTH MALE  
AND FEMALE  
ORGANS, SO THEY  
ORDINARILY  
FERTILIZE  
THEMSELVES.

UNLESS  
WE PRACTICE  
:AHEM:  
FAMILY PLANNING!

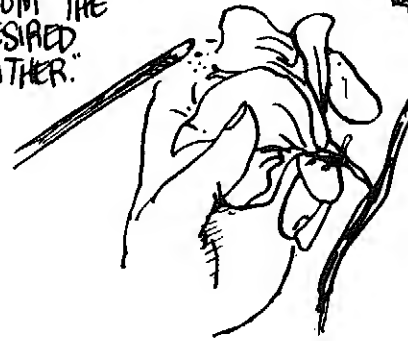


## HOW MENDEL MADE HYBRIDS:

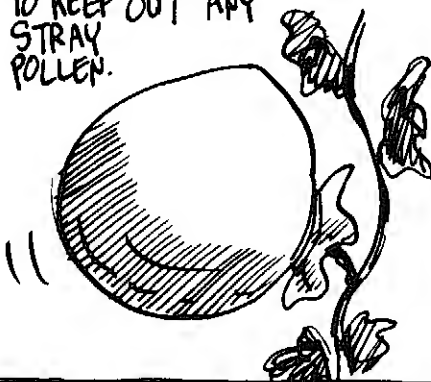
FIRST HE SNIPPED  
OFF THE ANTHERS  
WHILE STILL IMMATURE  
TO PREVENT  
"SELFING."



THEN HE DUSTED THE  
STIGMA WITH  
POLLEN TAKEN  
FROM THE  
DESIRED  
"FATHER."



FINALLY, HE TIED BAGS  
OVER THE FLOWERS  
TO KEEP OUT ANY  
STRAY POLLEN.



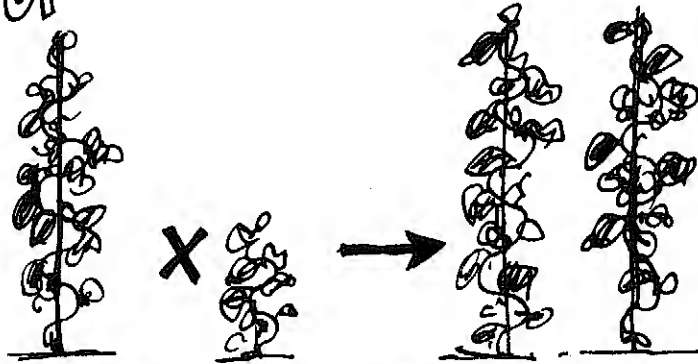
IN THIS  
WAY  
MENDEL  
WAS  
ABLE TO  
CONTROL  
THE  
PARENTAGE  
OF EACH  
GENERATION.

PSST!  
I THINK  
THE MONK  
IS PLAYING  
GOD!!





MENDEL'S FIRST MAJOR RESULT WAS THE DISCOVERY OF **DOMINANCE**. WHAT HAPPENED WHEN A TALL PLANT WAS CROSSED WITH A SHORT? ONE MIGHT EXPECT MEDIUM-SIZED PLANTS, **BUT**



IN FACT,  
ALL THE  
HYBRIDS  
WERE  
**TALL !!**

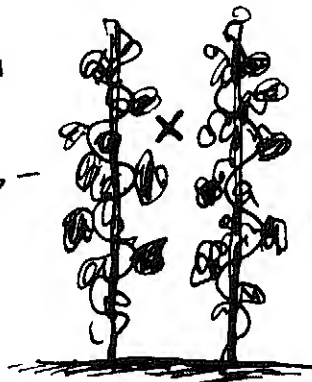
MENDEL EXPRESSED THIS BY SAYING THAT TALLNESS WAS **DOMINANT** OVER SHORTNESS (IN PEAS!). THE TRAIT OF SHORTNESS IS THEN CALLED **RECESSIVE**. IN EVERY CASE, ONE TRAIT WAS FOUND TO BE **DOMINANT**.



ROUND SEEDS ARE  
DOMINANT OVER WRINKLED;  
PLUMP PODS OVER  
PINCHED; GREY SEED  
COATS OVER WHITE  
SEED-COATS, ETC  
ETC ETC....

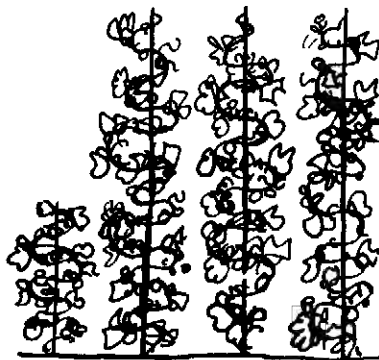
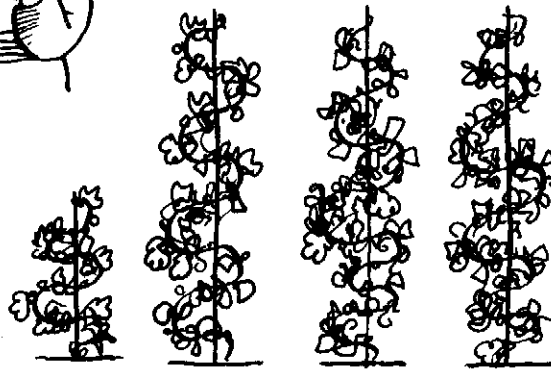
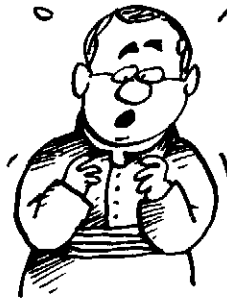
IT DIDN'T MATTER WHICH PARENT CONTRIBUTED THE POLLEN AND WHICH THE EGG. A TALL-SHORT HYBRID WAS ALWAYS TALL.

THE FUN  
BEGINS WHEN  
YOU START  
BREEDING  
THE HYBRIDS -



WHEN THE HYBRIDS  
SELF-FERTILIZED, ABOUT  
 $\frac{1}{4}$  OF THEIR OFFSPRING  
WERE SHORT.

THE RECESSIVE  
TRAIT REAPPEARED !!



CONTINUING THE  
SELF-FERTILIZATION,  
MENDEL FOUND THAT  
ABOUT ONE TALL IN  
THREE PRODUCED  
ONLY TALLS, WHILE  
THE OTHERS YIELDED  
BOTH TALLS AND  
SHORTS IN THE  
RATIO 3:1.  
THE SHORTS BRED  
ONLY SHORTS.

## MENDEL'S INTERPRETATION:

IT'S MATHEMATICAL!

THERE IS SOMETHING IN POLLEN AND EGG WHICH DETERMINES THE HEIGHT OF PEA PLANTS. THIS "SOMETHING" WE CALL A

# GENE.



EACH POLLEN GRAIN AND EGG HAS ONE HEIGHT GENE, SO THE PLANT FORMED BY THEIR UNION HAS TWO.

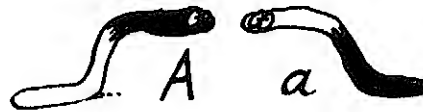
THE GENE MAY BE ONE OF TWO DISTINCT TYPES, OR

## ALLELES.

ONE ALLELE, A, IS FOR TALLNESS;  
THE OTHER ONE, a, IS FOR SHORTNESS.

GENES MAKE SHORTS?

CUT-OFFS...



A PLANT MAY HAVE THE SAME OR DIFFERENT ALLELES.



AA



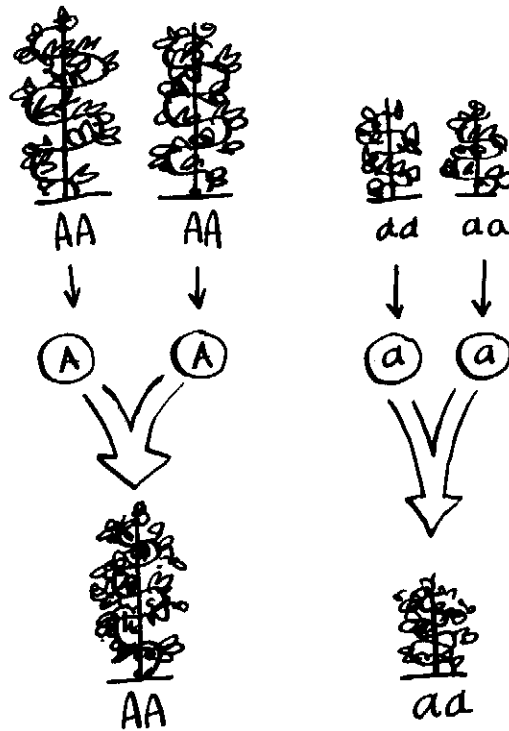
aa



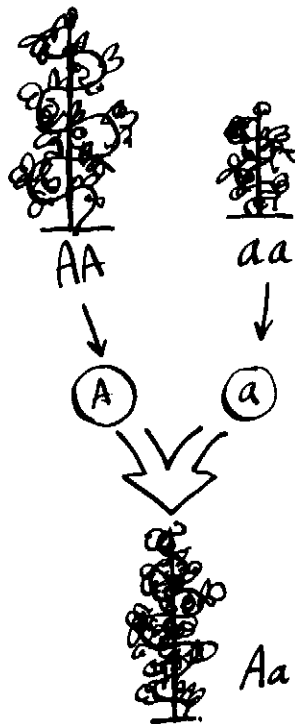
Aa

THE ALLELE A IS DOMINANT OVER a. THAT IS, THE PLANT WITH THE COMBINATION Aa IS TALL. THE ALLELES DO NOT "BLEND."

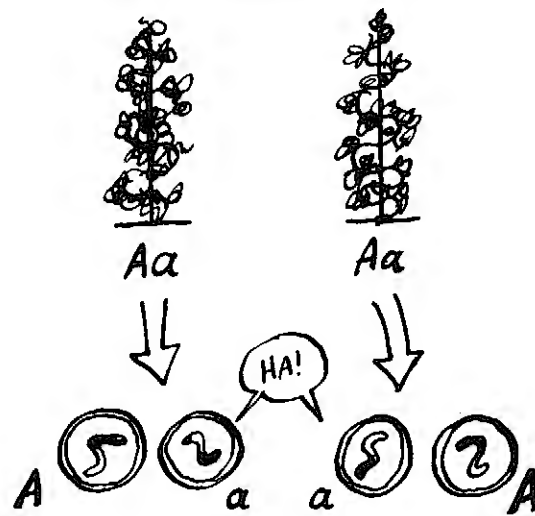
**W**HAT HAPPENS  
 WHEN AA  
 BREEDS WITH  
 AA? POLLEN AND  
 EGG EACH GET  
 ONE COPY OF  
 THE GENE...  
 IN THIS CASE,  
 THE ALLELES  
 ARE THE SAME -  
 A - SO THE  
 OFFSPRING WILL  
 AGAIN BE AA, OR  
 TALL. LIKewise,  
 aa CAN YIELD  
 ONLY aa. THESE  
 ARE THE STABLE  
 SHORT & TALL  
 VARIETIES.



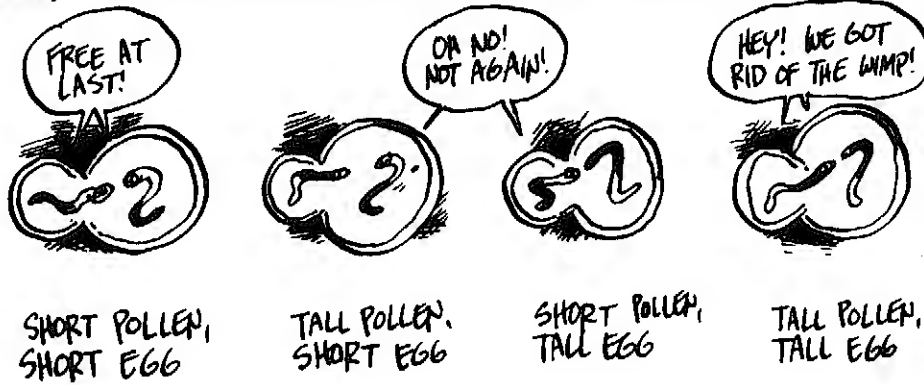
MENDEL'S FIRST  
 HYBRID WAS A  
 CROSS BETWEEN  
 AA AND aa:  
 THE POLLEN (OR EGG)  
 FROM AA CONTAINS  
 ONLY A, WHILE  
 THE EGG (OR POLLEN)  
 FROM aa CONTAINS  
 ONLY a.  
**RESULT:**  
 Aa, WHICH  
 IS TALL.



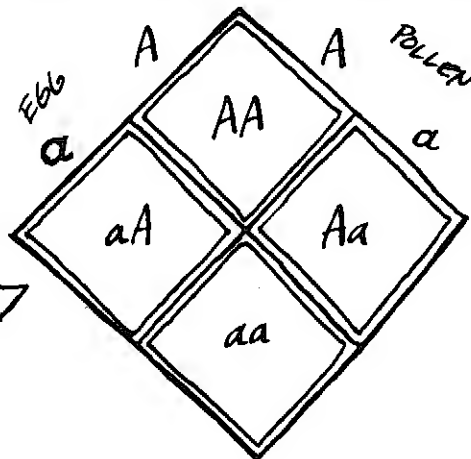
WHEN THE HYBRID  
SELF-FERTILIZES,  
ITS ALLELES  
A AND a ARE SORTED  
OUT RANDOMLY  
AMONG THE POLLEN  
GRAINS AND EGGS.  
BOTH A AND a  
APPEAR, AND IN  
ROUGHLY EQUAL  
PROPORTIONS.



WHEN EGGS AND POLLEN UNITE, THERE ARE FOUR POSSIBILITIES:



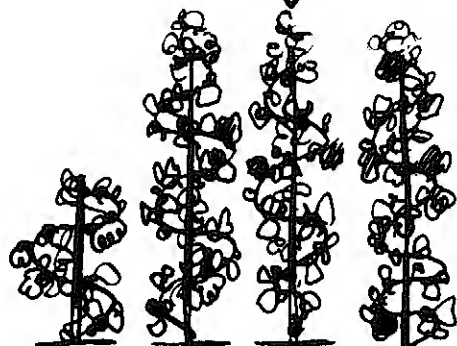
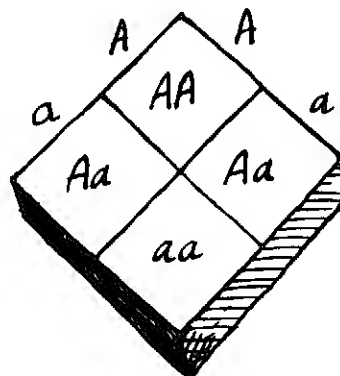
WHICH ARE  
SUMMARIZED IN  
THIS SQUARE:  
EACH POSSIBLE  
OFFSPRING  
APPEARS IN ONE  
OF THE  
SMALL  
BOXES.



HERE AGAIN ARE THE  
HYBRID'S DESCENDANTS,  
AS MENDEL OBSERVED  
THEM. THE FIRST  
GENERATION AGREES  
WITH THE CROSSING  
SQUARE:



$Aa$

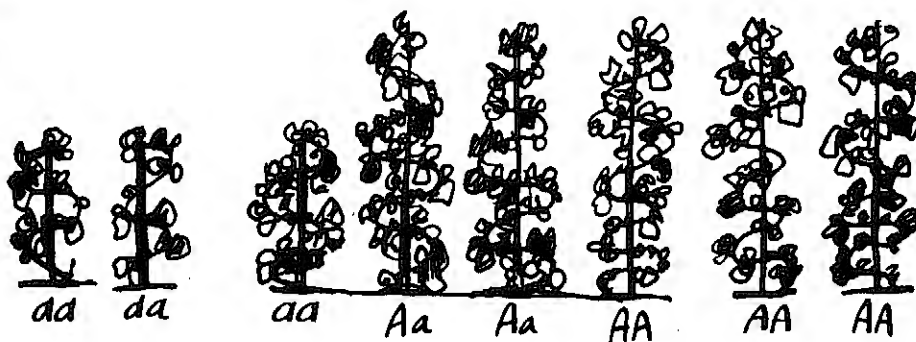
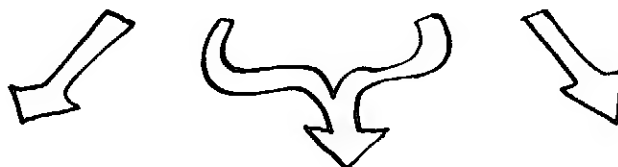


$aa$     $Aa$     $aA$     $AA$

$\frac{1}{4}$  TRUE-BREEDING  
TALLS ( $AA$ )

$\frac{1}{2}$  TALLS WHICH  
MAY BREED  
SHORTS ( $Aa$ )

$\frac{1}{4}$  TRUE-BREEDING  
SHORTS ( $aa$ )



$aa$

$aa$

$aa$

$Aa$

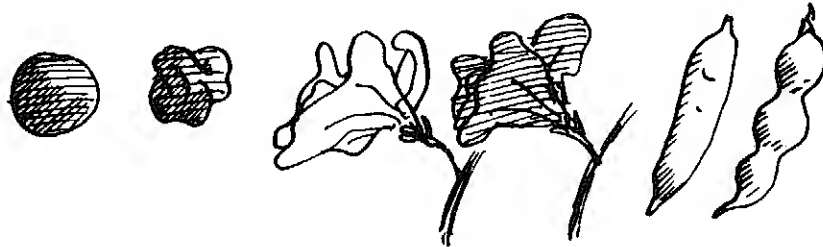
$Aa$

$AA$

$AA$

$AA$

MENDEL ALSO CROSSED SMOOTH-PEA PLANTS WITH WRINKLED, PURPLE FLOWERS WITH WHITE, ETC ETC ETC. IN EVERY CASE, HE FOUND THE CHARACTERISTIC TO BE CONTROLLED BY A SINGLE GENE WITH TWO DIFFERENT ALLELES, ONE OF WHICH WAS DOMINANT OVER THE OTHER.



SO IT SEEMED THAT POLLEN AND EGG WERE BOTH FULL OF THESE LITTLE "SOMETHINGS," ONE FOR EVERY HEREDITARY TRAIT OF THE ORGANISM. PRETTY CROWDED!



HOW CAN I DO MY JOB IN THIS MOB?

YOU DON'T HAVE TO: YOU'RE RECESSIVE!



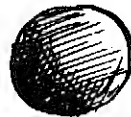
LORD KNOWS THEY MUST BE TINY!!

WITHOUT EVER SEEING A GENE, MENDEL CONCLUDED THAT HEREDITY IS CONTROLLED BY THESE "ATOMS OF INHERITANCE," WHICH NEVER BREAK OR BLEND, MAINTAINING THEIR CHARACTER FROM GENERATION TO GENERATION.

FINALLY, MENDEL MADE CROSSES BETWEEN PLANTS DIFFERING IN TWO CHARACTERISTICS — FOR EXAMPLE, A TALL PLANT WITH SMOOTH SEEDS AND A SHORT PLANT WITH WRINKLED SEEDS. THE QUESTION HERE IS: ARE HEIGHT AND SMOOTHNESS CORRELATED SOMEHOW, OR DO THEY ACT INDEPENDENTLY WHEN THE PLANT REPRODUCES??



CALL THE ALLELE FOR SMOOTH SEEDS  $S$ , AND THAT FOR WRINKLED SEEDS  $s$ .  $S$  IS DOMINANT, SO



$SS$

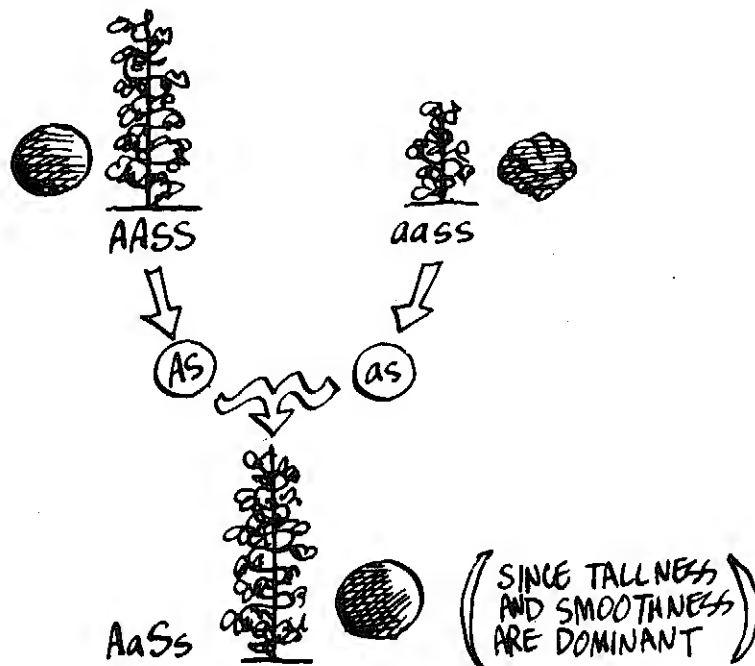


$Ss$



$ss$

THE CROSS IS BETWEEN  $AASS$  AND  $aass$ .

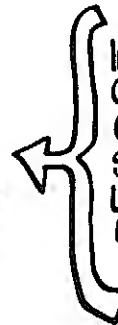
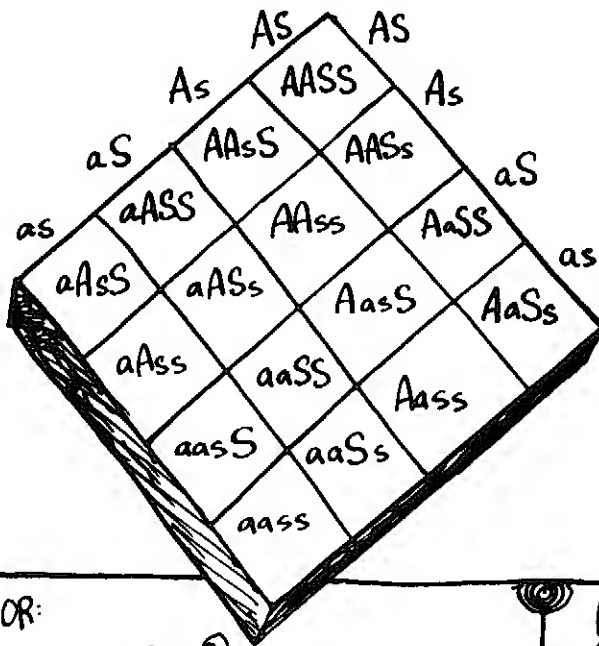




NOW FOR THE SELF-POLLINATION OF THE HYBRID:



THE GENES FOR HEIGHT AND SMOOTHNESS SORT OUT INDEPENDENTLY OF EACH OTHER, THEN ALL THESE POSSIBLE POLLENS AND EGGS WOULD BE EQUALLY LIKELY:



IN WHICH CASE, THE CROSSING SQUARE LOOKS LIKE THIS.

OR:

- |        |   |                   |
|--------|---|-------------------|
| 1 AASS | } | 9 TALL, SMOOTH    |
| 2 AASs |   |                   |
| 2 AaSS |   |                   |
| 4 AaSs |   |                   |
| 1 AAss | } | 3 TALL, WRINKLED  |
| 2 AaSS |   |                   |
| 1 aaSS | } | 3 SHORT, SMOOTH   |
| 2 aaSs |   |                   |
| 1 aass |   | 1 SHORT, WRINKLED |

AND THIS IS WHAT MENDEL OBSERVED — A RATIO OF 9:3:3:1. THIS EXPERIMENT, AND OTHERS WITH DIFFERENT COMBINATIONS, PROVED THE **PRINCIPLE OF INDEPENDENT ASSORTMENT**: THE ALLELES OF ONE GENE SORT OUT INDEPENDENTLY OF THE ALLELES OF ANOTHER. (WE'LL SOON SEE THAT THIS 'PRINCIPLE' ISN'T QUITE TRUE!)

NOW THAT WE'VE SEEN  
HOW GENES WORK,  
HERE'S A BIT OF  
GENETICS JARGON,  
IN CASE YOU SHOULD  
EVER WANT TO  
EAVESDROP ON A  
MODERN GENETICIST...



THIS GEN-TEK DEAL  
MEANS ELEPHANT  
BUCKS, BABY... WE'RE  
TALKING RECOMBINANT  
BANK ACCOUNTS,  
PROFESSOR...

WELL... NOT THAT KIND  
OF JARGON...

GENETICISTS DISTINGUISH  
BETWEEN AN ORGANISM'S  
**PHENOTYPE** - WHAT IT  
LOOKS LIKE - AND ITS  
**GENOTYPE** - WHAT  
ALLELES IT HAS.



AA



Aa

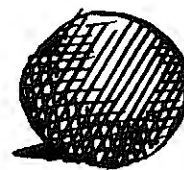
SAME  
PHENOTYPE,  
DIFFERENT  
GENOTYPE

AN ORGANISM IS  
**HOMOZYGOUS** WITH  
RESPECT TO A  
GIVEN GENE IF ITS  
TWO ALLELES ARE  
THE SAME, AND  
**HETEROZYGOUS**  
IF THEY'RE  
DIFFERENT.



SS

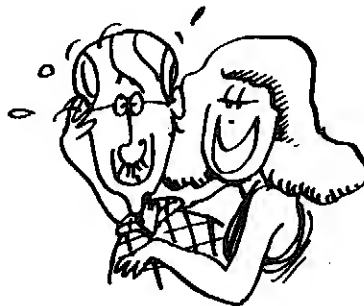
HOMOZYGOUS



Ss

HETEROZYGOUS

SO NOW YOU KNOW  
WHAT A GENETICIST  
MEANS BY  
"PHENOTYPICALLY SMOOTH,  
GENOTYPICALLY  
HETEROZYGOUS."



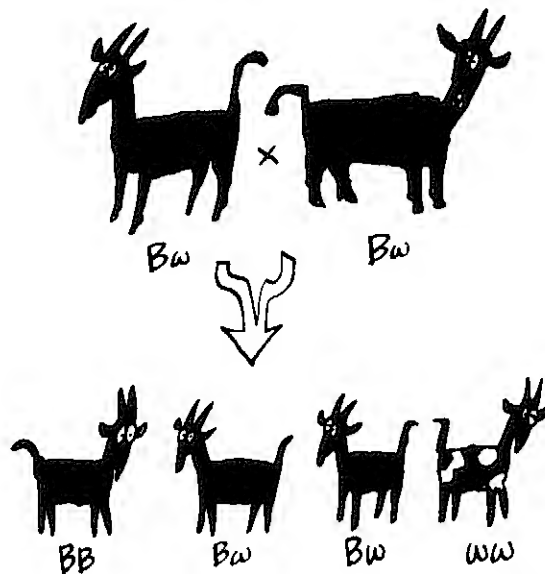
YES...  
NOW TELL  
ME ABOUT  
RECOMBINANT  
BANK  
ACCOUNTS...

INCIDENTALLY — WE'RE NOW IN A POSITION TO UNDERSTAND JACOB'S SPECKLED FLOCK:



SPELL IT OUT FOR ME!

THE ALLELE FOR A BLACK COAT, CALL IT B, WAS DOMINANT. THERE WAS ALSO A RECESSIVE ALLELE, w, FOR WHITE SPECKLES. MANY OF LABAN'S PHENOTYPICALLY BLACK ANIMALS SECRETLY HARBORED THIS w, SO THEIR KIDS WERE SOMETIMES SPECKLED.\*



IN OTHER WORDS —

THOSE GOATS WERE HETEROZY-GOATS!



\* ACTUALLY, THE GENETICS OF COAT COLOR ARE MORE COMPLEX, BUT THE PRINCIPLE IS THE SAME: RECESSIVE ALLELES.

# QUESTION:

IF YOU SEE A DOMINANT PHENOTYPE, HOW CAN YOU TELL IF IT'S A HETEROZYGOTE?

IS IT POLITE TO ASK?



FOR INSTANCE, IN HUMANS BROWN EYES ARE DOMINANT OVER BLUE. CALL THE GENES  $B$  AND  $b$ , RESPECTIVELY.



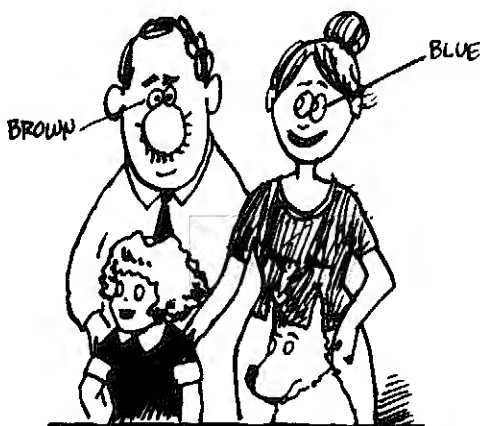
HOW CAN WE TELL IF THIS BROWN-EYED PERSON IS  $BB$  OR  $Bb$ ?

ONE WAY IS TO CROSS HIM WITH A RECESSIVE HOMOZYGOTE— I.E., A BLUE-EYED PERSON,  $bb$ .



SORRY... I HAVE TO BACK OUT OF THIS EXPERIMENT... MONK'S VOWS, YOU KNOW...

O.K... WE'LL USE SOMEBODY ELSE...



IF ANY OF THE LITTLE HYBRIDS HAS BLUE EYES, THE BROWN-EYED PARENT MUST HAVE BEEN A **HETEROZYGOTE**,  $Bb$ . IF HE HAD BEEN  $BB$ , ALL THE CHILDREN WOULD HAVE BEEN  $Bb$ , WITH BROWN EYES.

FOR EXAMPLE, MY FIRST  
WIFE HAS BROWN EYES, AND I HAVE  
BLUE EYES. ONE OF OUR SONS  
HAS BLUE EYES; ONE HAS BROWN  
EYES. THEREFORE, MY FIRST  
WIFE MUST BE HETEROZYGOUS.  
(THE BLUE-EYED BOY MUST HAVE  
ONE ALLELE FROM HER.)  
TRY DOING THE SQUARE!



MY SECOND WIFE HAS BLUE EYES LIKE ME. IF OUR CHILD HAD  
BROWN EYES, WHAT WOULD WE MAKE OF THAT? BETTER  
ASK THE MILKMAN!!



SOME EXAMPLES  
OF DOMINANT AND  
RECESSIVE GENES  
IN HUMANS:



★ BROWN EYES ARE  
DOMINANT OVER BLUE  
EYES.

★ COLOR VISION IS  
DOMINANT OVER COLOR  
BLINDNESS.

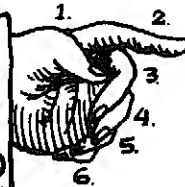
★ HAIRY HEADS ARE  
DOMINANT OVER BALD  
ONES.

★ THE ABILITY TO CURL  
THE TONGUE IS DOMINANT  
OVER THE INABILITY TO  
CURL THE TONGUE.

★ EXTRA FINGERS ARE  
DOMINANT OVER FIVE  
FINGERS (ODD BUT TRUE!).

★ DOUBLE DOSE OF RECESSIVES  
ALSO CAUSE SUCH  
RARE DISEASES AS HEMO-  
PHILIA, SICKLE-CELL ANEMIA,  
TAY-SACHS SYNDROME,  
THALASSEMIA, DWARFISM...

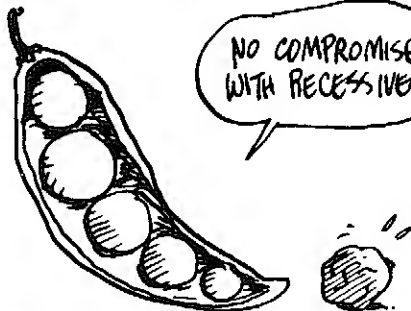
TO SUM  
UP...





MY PRINCIPAL RESULTS:

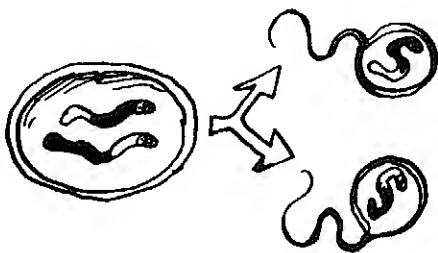
**1** HEREDITARY TRAITS ARE GOVERNED BY GENES WHICH RETAIN THEIR IDENTITY IN HYBRIDS. GENES ARE NEVER BLENDED TOGETHER.



**2** ONE FORM ("ALLELE") OF A GENE MAY BE DOMINANT OVER ANOTHER. BUT RECESSIVE GENES WILL POP UP LATER !!



**3** EACH ADULT ORGANISM HAS TWO COPIES OF EACH GENE — ONE FROM EACH PARENT. WHEN POLLEN OR SPERM AND EGGS ARE PRODUCED, THEY EACH GET ONE COPY.



**4** DIFFERENT ALLELES ARE SORTED OUT TO SPERM AND EGG RANDOMLY AND INDEPENDENTLY. ALL COMBINATIONS OF ALLELES ARE EQUALLY LIKELY:

AABBCCDDEEFFGGHH  
AaBBCCDDEEFFGGHH  
aABBCCDDEEFFGGHH  
aaBBCCDDEEFFGGHH  
AAbbCCDDEEFFGGHH  
AABbCCDDEEFFGGHH  
AaBbCCDDEEFFGGHH  
aaBbCCDDEEFFGGHH

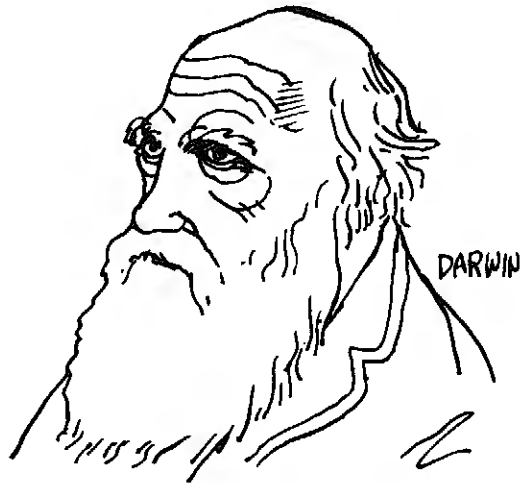


➔ WE'LL SEE SHORTLY THAT NOT ALL THESE POINTS ARE EXACTLY CORRECT... DOMINANCE IS SOMETIMES ONLY PARTIAL... THERE ARE ORGANISMS WITH ONLY A SINGLE SET OF GENES... AND SOME WITH FOUR SETS... AND DEVIATIONS FROM INDEPENDENT ASSORTMENT TURN OUT TO BE VERY IMPORTANT...

MENDEL PRESENTED HIS THEORY IN 1865 TO THE BRÜNN NATURAL SCIENCE SOCIETY... IT PUT THEM TO SLEEP.



UNFORTUNATELY, NOBODY CARED ABOUT THE PROBLEM ANY MORE... IT HAD GONE OUT OF FASHION... AND, BESIDES, SINCE 1859, BIOLOGISTS HAD BEEN DISTRACTED BY THE NEW THEORY OF EVOLUTION, AND COULDN'T BE BOTHERED WITH MENDEL'S EQUATIONS.



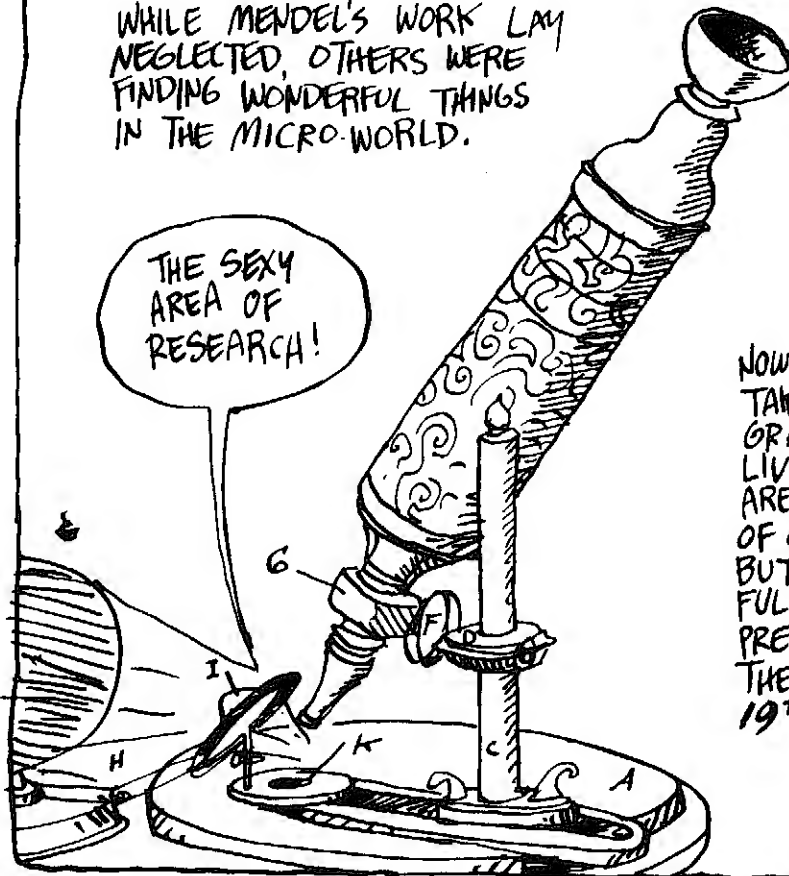
BY THE TIME MENDEL DIED, THE SCIENTIFIC COMMUNITY HAD TOTALLY FORGOTTEN HIS WORK. "MY TIME WILL COME," HE SAID, NOT LONG BEFORE HIS DEATH IN 1884...





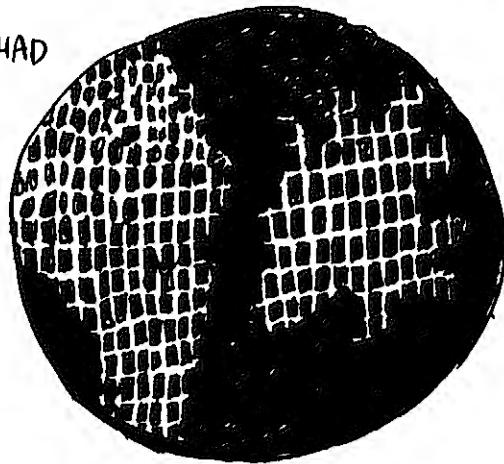
# NOW YOU SEE THEM...

WHILE MENDEL'S WORK LAY NEGLECTED, OTHERS WERE FINDING WONDERFUL THINGS IN THE MICRO-WORLD.

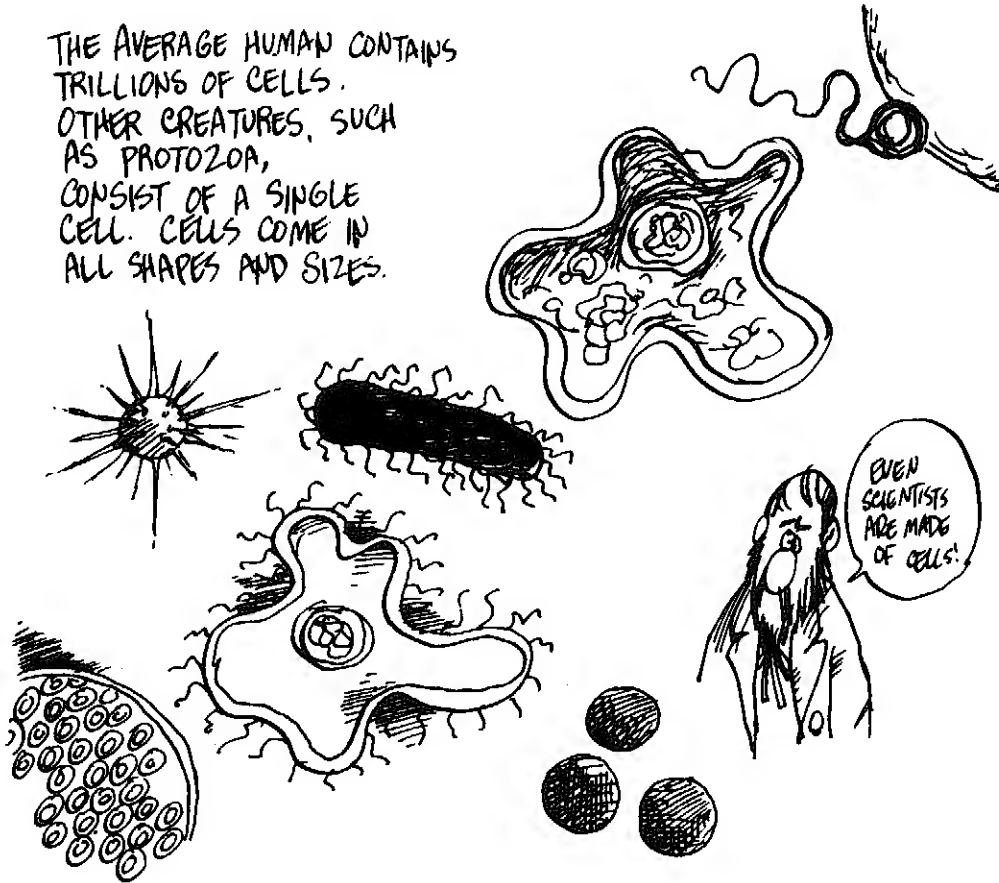


NOWADAYS, WE TAKE IT FOR GRANTED THAT ALL LIVING THINGS ARE MADE UP OF **CELLS** — BUT THIS WASN'T FULLY APPRECIATED UNTIL THE LATE 19<sup>TH</sup> CENTURY.

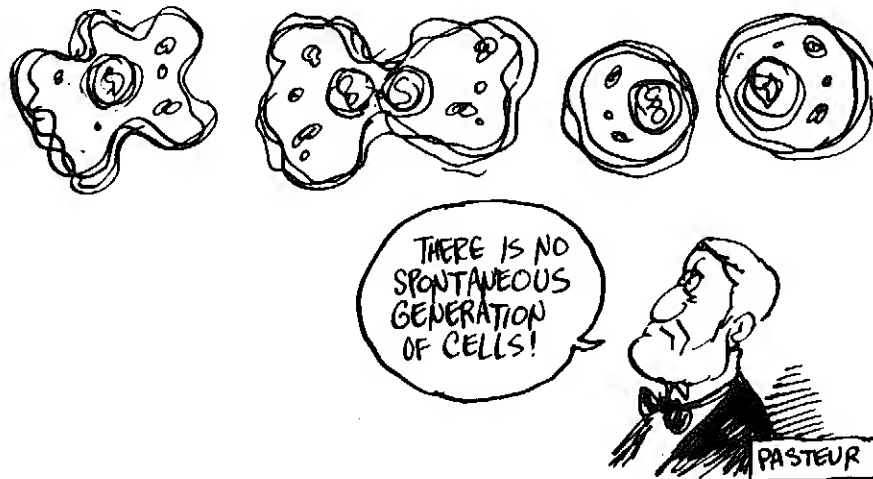
AS FAR BACK AS THE 1600'S, ROBERT HOOKE (1635-1703) HAD NOTICED THE CELLULAR STRUCTURE OF CORK. BUT IT WASN'T UNTIL THE 1800'S THAT SCIENTISTS, ARMED WITH BETTER MICROSCOPES, REALIZED THAT ALL OF US ARE DIVIDED INTO LITTLE COMPARTMENTS.



THE AVERAGE HUMAN CONTAINS TRILLIONS OF CELLS. OTHER CREATURES, SUCH AS PROTOZOA, CONSIST OF A SINGLE CELL. CELLS COME IN ALL SHAPES AND SIZES.



MOREOVER, SCIENTISTS SAW THAT ALL CELLS COME FROM THE **DIVISION** OF A PRE-EXISTING CELL. BEFORE DIVISION, EVERYTHING IN THE CELL IS DOUBLED.

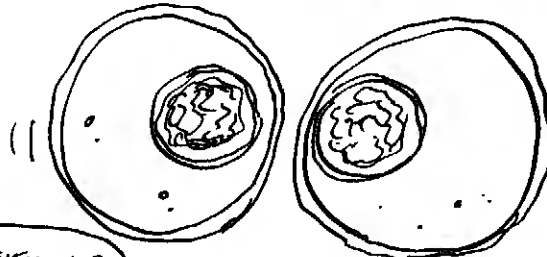
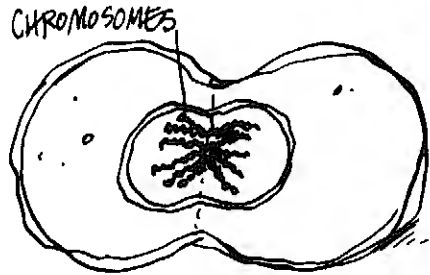
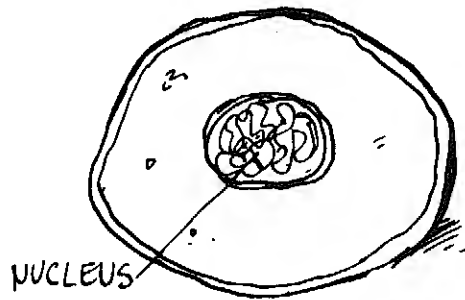


AS MICROSCOPES IMPROVED, THE CELL'S INTERNAL STRUCTURE EMERGED...

FIRST OF ALL, THERE WAS THE **NUCLEUS**— AND WITHIN THE NUCLEUS WAS SOMETHING WEIRD..

JUST BEFORE CELL DIVISION, SOME SHORT, STRINGY OBJECTS SUDDENLY APPEARED, DOUBLED, AND THEN VANISHED!

THESE WERE DUBBED "**CHROMOSOMES**" AND WERE THE CAUSE OF MUCH DEBATE!!



CHROMOSOMES ARE LIKE CAMPAIGN PROMISES— THEY MATERIALIZE FROM THE AIR AND THEN DISAPPEAR...

THEY SLIP IN AND OUT THE BACK DOOR— LIKE A MILITARY!

ONLY ONE WAY TO FIND OUT..

CONSULT AN EXPERT!

AN EXPERT IN CELLS?

NO... AN EXPERT IN DISAPPEARANCES!

ONLY ONE POSSIBILITY, GENTS!

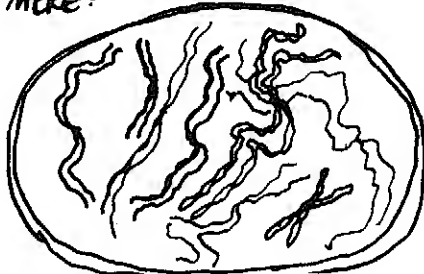
THEY WERE THERE ALL ALONG!

IT WAS FINALLY AGREED— CHROMOSOMES DON'T REALLY DE-MATERIALIZE OR DISSOLVE. THEY'RE JUST TOO **SKINNY** MOST OF THE TIME TO BE VISIBLE WITH A CONVENTIONAL MICROSCOPE. DURING CELL DIVISION, HOWEVER, THEY **COIL UP**, BECOMING THICK ENOUGH TO SEE.

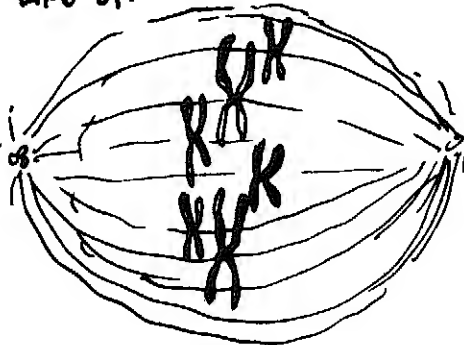


CAREFUL STUDY REVEALED WHAT HAPPENS TO CHROMOSOMES DURING CELL DIVISION.

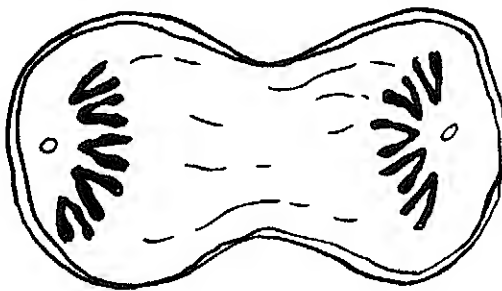
FIRST—WHILE STILL INVISIBLE—THE CHROMOSOMES DUPLICATE THEMSELVES, REMAINING ATTACHED AT A SPOT CALLED THE CENTROMERE:



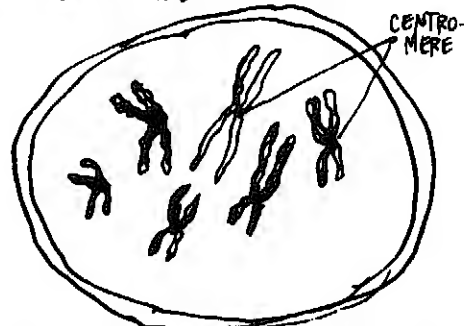
THE MEMBRANE AROUND THE NUCLEUS DISSOLVES, AND A FIBROUS SPINDLE FORMS, ON WHICH THE CHROMOSOMES LINE UP.



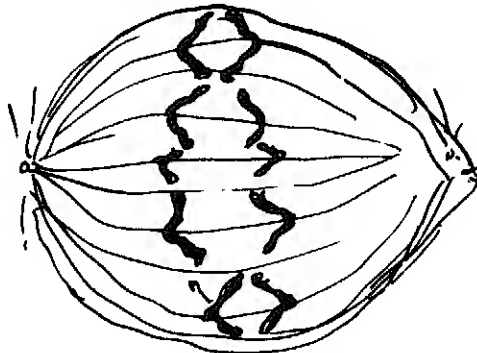
THE CHROMOSOMES ARRIVE AT THE OPPOSITE POLES, AND THE SPINDLE DISPERSES.



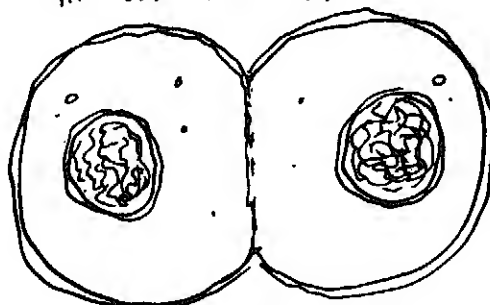
NEXT THEY THICKEN AND SHORTEN, BECOMING VISIBLE UNDER THE MICROSCOPE.



THE CENTROMERES DIVIDE AS THE SPINDLE FIBERS TUG THE CHROMOSOME PAIRS APART.

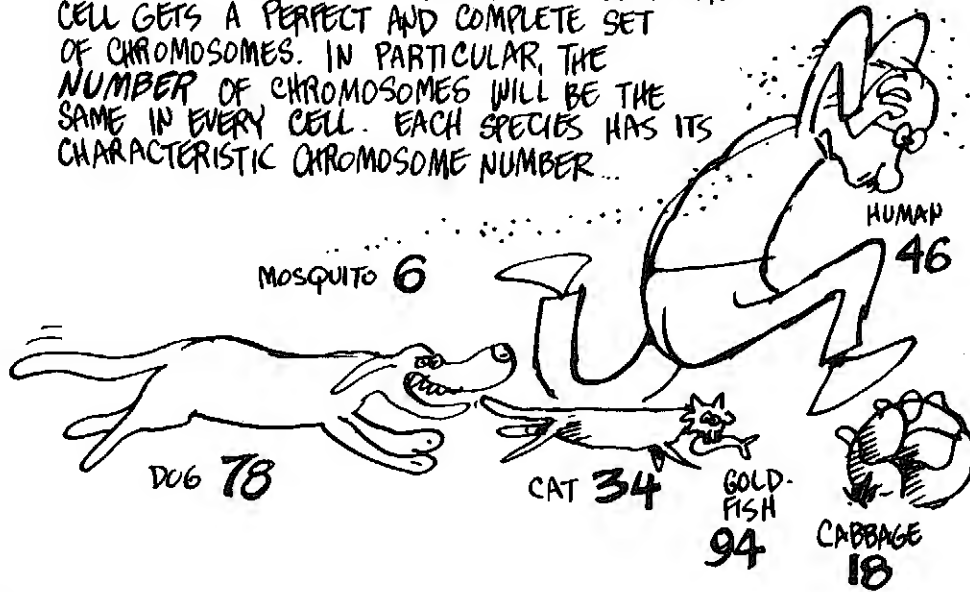


THE NUCLEAR MEMBRANE RE-FORMS; THE CHROMOSOMES UNWIND INTO INVISIBILITY; AND THE CELL DIVIDES.

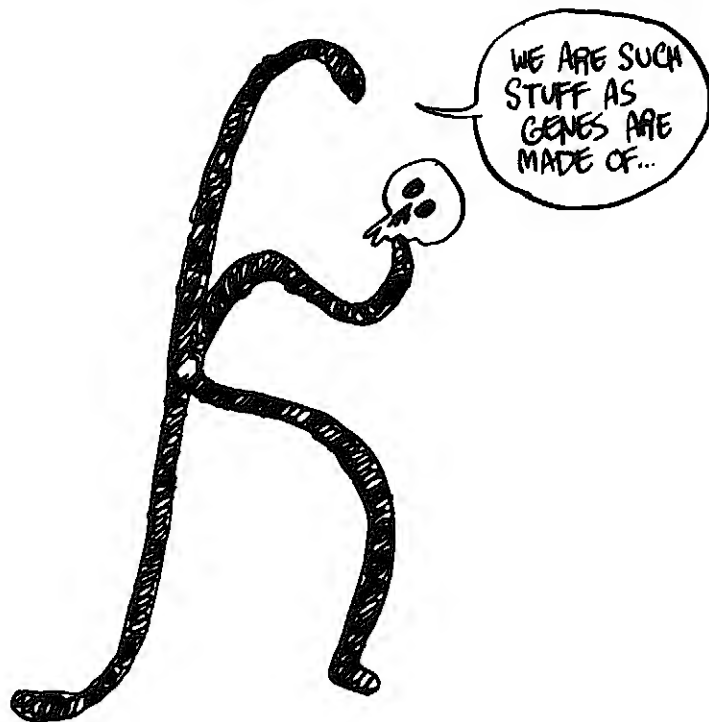


THIS PROCESS IS CALLED **MITOSIS**.

THE PROCESS OF MITOSIS IS EXTREMELY ACCURATE. IT ENSURES THAT EVERY "DAUGHTER" CELL GETS A PERFECT AND COMPLETE SET OF CHROMOSOMES. IN PARTICULAR, THE NUMBER OF CHROMOSOMES WILL BE THE SAME IN EVERY CELL. EACH SPECIES HAS ITS CHARACTERISTIC CHROMOSOME NUMBER...



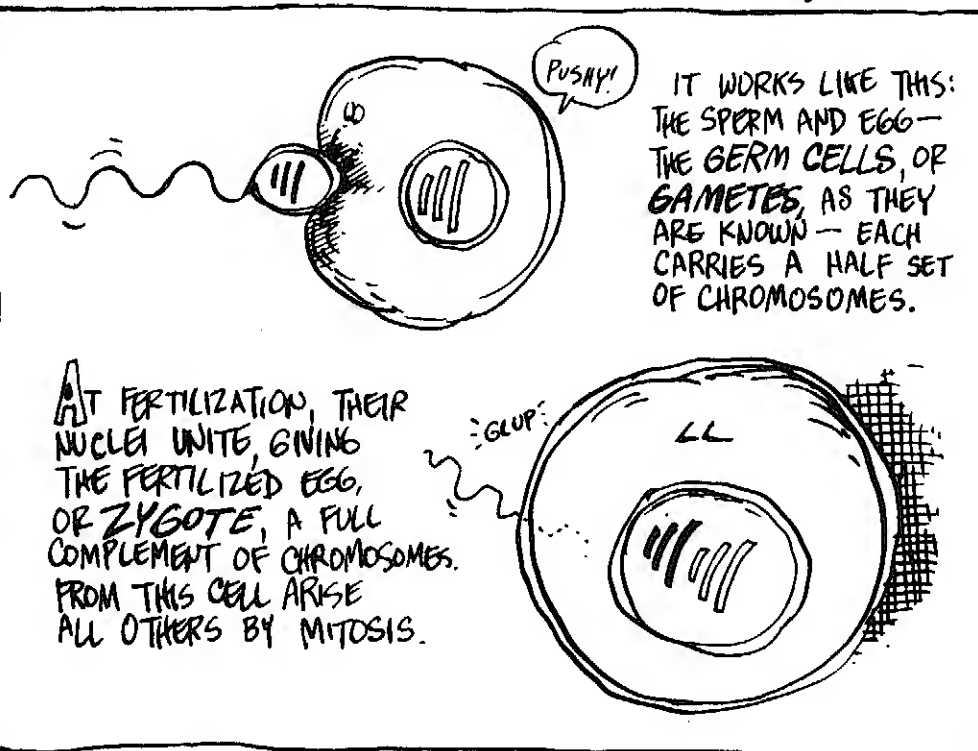
YOU MAY HAVE NOTICED THAT ALL THESE NUMBERS ARE EVEN. THERE IS A GOOD REASON FOR THIS — A REASON THAT POINTS TO THE CHROMOSOMES AS THE VERY MATERIAL OF HEREDITY ITSELF!

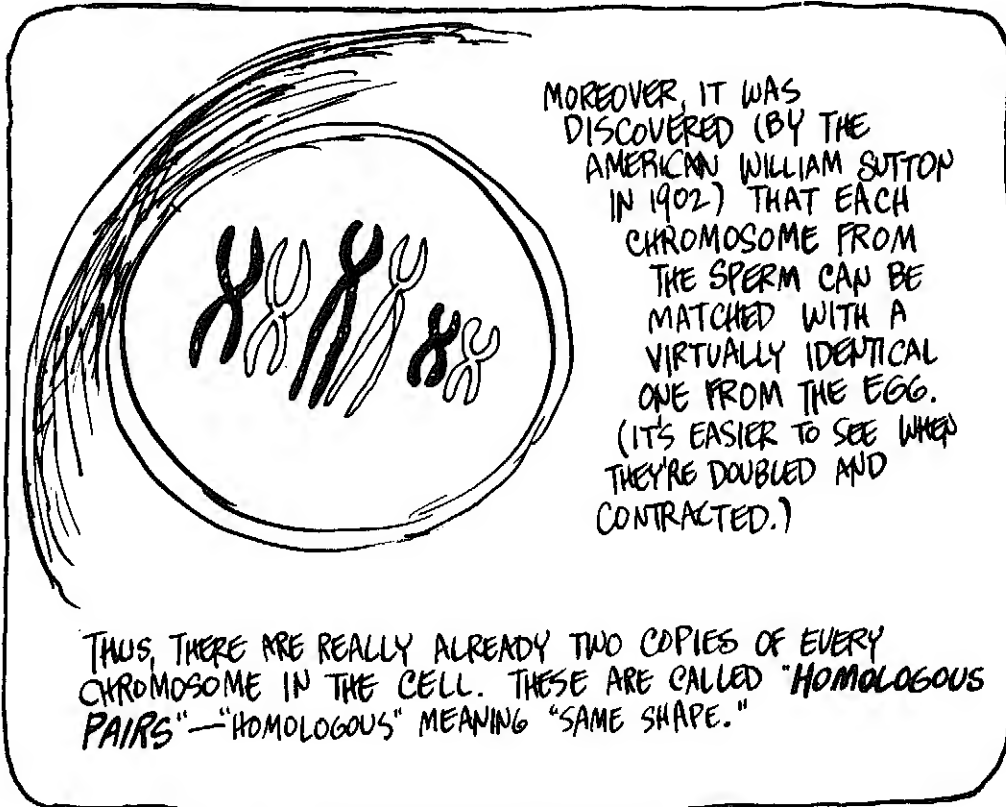


IT WAS THIS  
**FACT:**

SPERM AND EGG ARE  
SINGLE CELLS WITH  
ONLY HALF THE NORMAL  
NUMBER OF CHROMOSOMES.

DAZZLING!



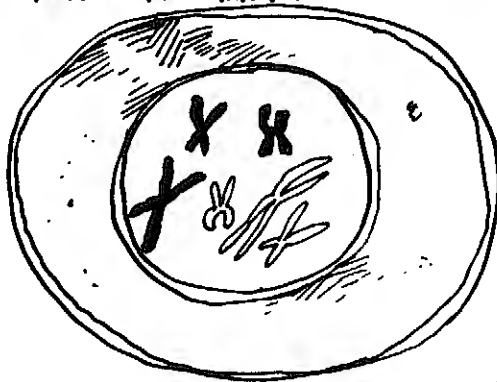


HUMANS, FOR EXAMPLE, WITH 46 CHROMOSOMES, REALLY HAVE 23\* HOMOLOGOUS PAIRS: ONE FROM EACH PAIR COMES FROM MOM AND ONE FROM DAD.



THIS PROCESS, CALLED **MEIOSIS**, IS ACTUALLY A **DOUBLE** DIVISION:

AS IN MITOSIS, THE CHROMOSOMES DOUBLE AND THICKEN:



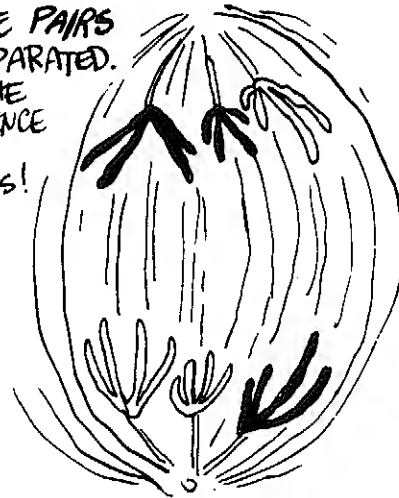
BUT THEN THE **HOMOLOGOUS** CHROMOSOMES PAIR OFF -- SOMEHOW!



AGAIN THE SPINDLE FIBERS FORM AND THE CHROMOSOME QUARTETS ("TETRADES") LINE UP...



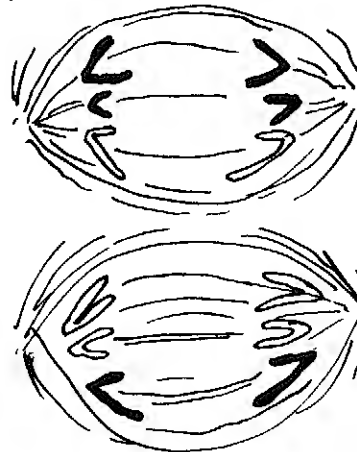
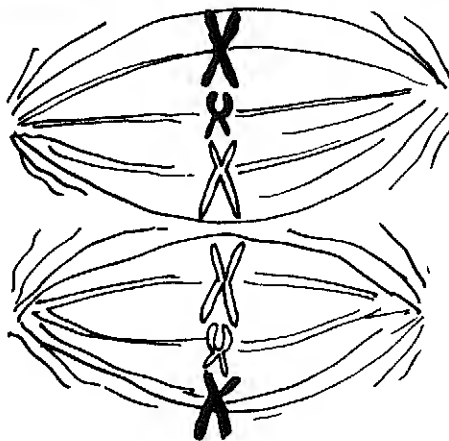
AND THE **PAIRS** ARE SEPARATED. NOTE THE DIFFERENCE FROM MITOSIS!



(MORE ON THIS LATER!)

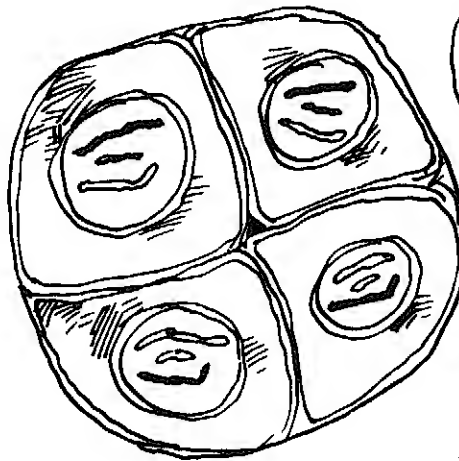
WHEN THEY REACH THE POLES, THE SPINDLE VANISHES AND NEW SPINDLES FORM "THE OTHER WAY."

THE CHROMOSOMES THEN SEPARATE, AS IN MITOSIS.





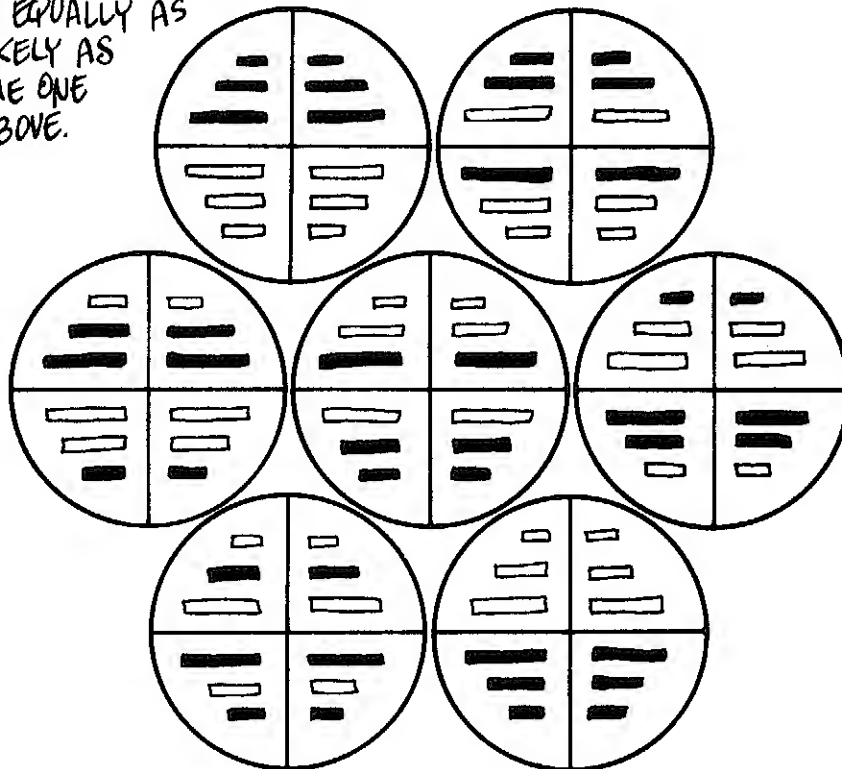
MEIOSIS RESULTS  
IN **FOUR** CELLS,  
EACH WITH **HALF**  
THE CHROMOSOMES  
OF THE ORIGINAL.  
COUNT 'EM —  
3 VS. 6 IN THIS  
CASE.



BUT ALWAYS  
ONE FROM EACH  
HOMOLOGOUS  
PAIR!



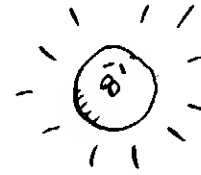
NOTE THAT WHICH COPY ("HOMOLOG") OF EACH CHROMOSOME GOES  
TO WHICH CELL IS COMPLETELY RANDOM.  
EACH OF THESE COMBINATIONS  
IS EQUALLY AS  
LIKELY AS  
THE ONE  
ABOVE.



THAT IS, THE CHROMOSOMES OBEY THE LAW OF  
INDEPENDENT ASSORTMENT.



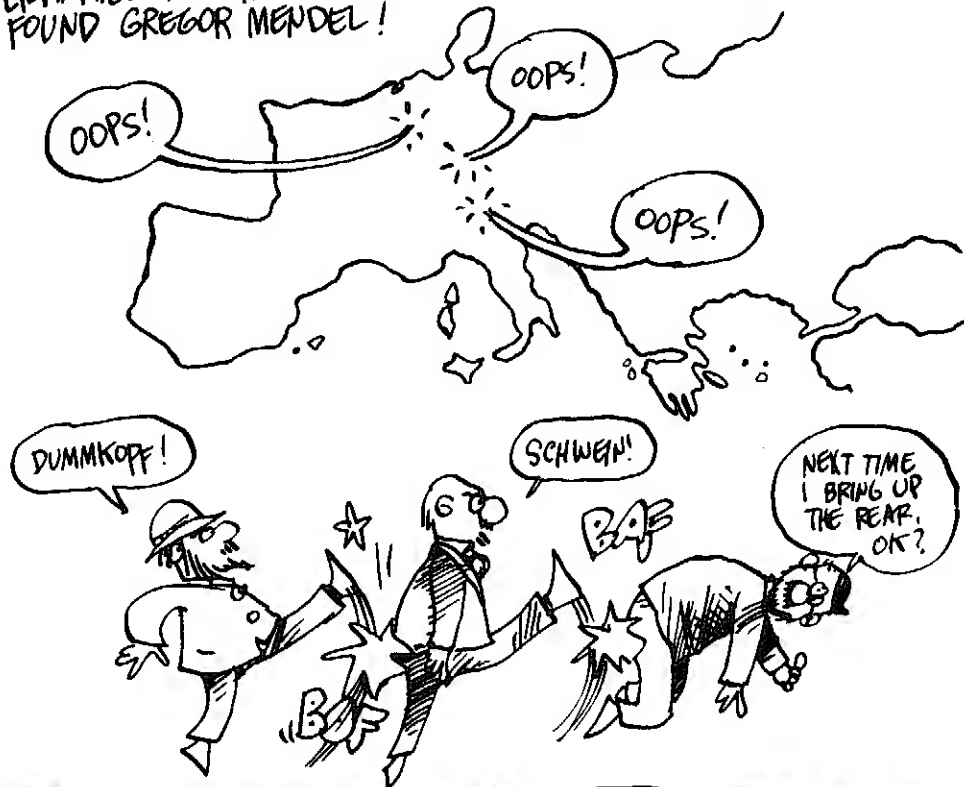
ONCE MEIOSIS AND MITOSIS WERE UNDERSTOOD, BIOLOGISTS BEGAN TO SUSPECT THAT CHROMOSOMES MIGHT GOVERN HEREDITY... THEY LOOKED AGAIN AT PATTERNS OF INHERITANCE... AND SCIENCE AGAIN MARCHED — BACKWARD, TO THE LAWS OF MENDEL!!



TOWARD THE END OF THE 19<sup>TH</sup> CENTURY, THREE SCIENTISTS, WORKING INDEPENDENTLY, MORE OR LESS DUPLICATED THE AUSTRIAN MONK'S EXPERIMENTS AND RESULTS. THEY WERE:



IN THE YEAR 1900, ALL THREE SEARCHED THE SCIENTIFIC LIBRARIES FOR PRECURSORS OF THEIR OWN WORK, AND ALL FOUND GREGOR MENDEL!



AFTER THEY HAD FINISHED KICKING THEMSELVES, DEVRIES, CORRENS AND TSCHERMAK ANNOUNCED MENDEL'S DISCOVERY TO THE WORLD. WITHIN TWO YEARS, WILLIAM SUTTON HAD SEEN HOMOLOGOUS PAIRS OF CHROMOSOMES IN GRASSHOPPER CELLS, AND SCIENCE HAD SEEN THE LIGHT!!



TO SUMMARIZE:

WHAT ~~EXACTLY~~ DID THEY REALIZE?

ANSWER:



CHROMOSOMES BEHAVE LIKE GENES. THEY RETAIN THEIR IDENTITY IN HYBRIDS, AND THEY SEGREGATE INDEPENDENTLY WHEN GERM CELLS ARE MADE. THEREFORE, IT'S LOGICAL TO ASSUME THAT GENES LIE ON CHROMOSOMES. (THERE MUST BE MANY GENES ON EACH ONE, BECAUSE THERE MUST BE FAR MORE GENES THAN THE FEW DOZEN CHROMOSOMES TYPICAL OF MOST SPECIES.)

A B c d E f ETC!

THE DISCOVERY OF HOMOLOGOUS PAIRS REALLY CINCHED THE CONNECTION TO MENDEL'S FINDINGS. REMEMBER, EACH CELL HAS A PAIR OF ALLELES FOR EACH GENE. NOW IT WAS REALIZED THAT:



THE TWO COPIES OF A GIVEN GENE LIE AT THE SAME POINT ON HOMOLOGOUS CHROMOSOMES.

I.E., IF ONE GENE FOR HEIGHT LIES HERE →



THEN THE OTHER COPY MUST BE HERE ←

ALL THIS TURNS OUT TO BE TRUE... BUT ONCE PEOPLE LOOKED MORE DEEPLY INTO THE MATTER, THEY DISCOVERED A FEW THINGS MENDEL HADN'T REALIZED...

FOR ONE THING, NOT ALL ORGANISMS HAVE A DOUBLE SET OF CHROMOSOMES. MANY LOWER SPECIES, LIKE SOME FUNGI, HAVE JUST A SINGLE SET.

LOWER THAN WHOM?

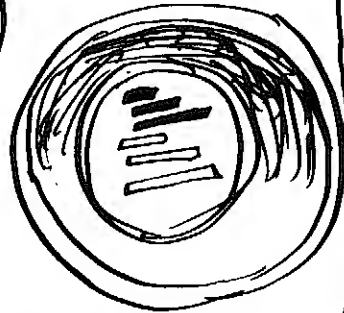


A CELL WITH A SINGLE SET OF CHROMOSOMES IS CALLED **HAPLOID**; ONE WITH TWO SETS IS CALLED **DIPLOID**. OUR BODY CELLS ARE DIPLOID, WHILE OUR GERM (SEX) CELLS ARE HAPLOID.



HAPLOID

DIPLOID



DIPLOID ORGANISMS INCLUDE ALL THE FAMILIAR MAMMALS AND BIRDS AND MANY PLANTS. HAPLOIDS INCLUDE MALE HONEY BEES, MANY FUNGI, AND ASEXUAL ONE-CELLED CREATURES.

BESIDES ALL THESE, THERE ARE ALSO **POLYPLOID** ORGANISMS, WITH MULTIPLE SETS OF CHROMOSOMES. A SURPRISING NUMBER OF EVERYDAY PLANTS ARE POLYPLOID. (NOT PEAS, THOUGH!!)

LIKE THE POTATO!



THE OTHER MAIN PROBLEM WITH MENDEL'S THEORY WAS THE PRINCIPLE OF INDEPENDENT ASSORTMENT. A PRECISE MEASURE OF HOW WRONG IT WAS LED TO THE ABILITY TO MAP OUT EXACTLY WHERE ON THE CHROMOSOME EACH OF ITS GENES MIGHT LIE... READ ON...



# MAPMAKING

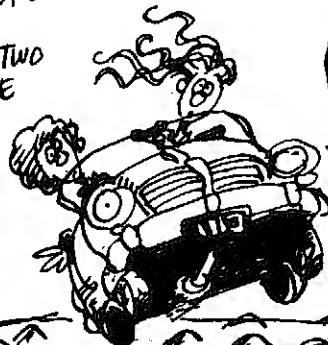
TO MENDEL—AND HIS  
HEIRS—GENES WERE  
JUST ABSTRACTIONS,  
LETTERS YOU COULD JUGGLE  
TO EXPLAIN AND PREDICT  
HOW HEREDITARY QUALITIES  
WOULD BE PASSED  
ALONG TO FUTURE  
GENERATIONS.

NOW IT APPEARED THAT  
GENES WERE ACTUAL,  
PHYSICAL OBJECTS. THEY  
LAY IN SOME ORDER ALONG  
THE CHROMOSOMES OF  
EVERY CELL, AND THE TWO  
ALLELES OF EACH GENE  
WERE ON THE TWO  
CHROMOSOMES OF A  
HOMOLOGOUS PAIR.

THEY'RE LIKE  
**GHOSTS**—  
INFLUENTIAL  
BUT  
INSUBSTANTIAL!



THEY'RE  
AS REAL AS  
BUMPS IN  
THE ROAD!



ONE MIGHT WONDER  
IF IT'S POSSIBLE TO  
MAKE A **GENE MAP**  
SHOWING JUST WHERE  
ON EACH CHROMO-  
SOME ALL THESE  
HEREDITARY UNITS  
MIGHT LIE!!

THE ANSWER TO THIS DEPENDS ON A SEEMING **PARADOX**, FOR IN ONE RESPECT MENDEL'S FINDINGS CONFLICTED WITH THE OBSERVED BEHAVIOR OF CHROMOSOMES...



NAMELY —  
THE PRINCIPLE OF  
INDEPENDENT  
ASSORTMENT!

OBSERVE: THE NUMBER OF GENES MUST BE TREMENDOUS TO GOVERN A COMPLEX ORGANISM, BUT THE NUMBER OF CHROMOSOMES IN A CELL IS FAIRLY SMALL. A PEA PLANT HAS JUST **7 PAIRS** OF CHROMOSOMES, A HUMAN **23**.

CONCLUSION:  
MANY GENES  
ON EACH  
CHROMOSOME!



THE PROBLEM: IF TWO GENES LIE ON THE SAME CHROMOSOME, **HOW CAN THEY BE INDEPENDENT??** AFTER ALL, CHROMOSOMES DON'T BREAK APART, DO THEY? SHOULDN'T DIFFERENT GENES SOMETIMES BE **LINKED??**

PHYSICALLY  
LINKED — BY THE  
CHROMOSOME!



SO — DO GENES  
ASSORT INDEPEN-  
DENTLY OR NOT?

WELL, IT TURNED OUT  
TO BE SORT OF HALF-AND-HALF...



THERE IS LINKAGE BETWEEN CERTAIN  
GENES...

**BUT**



CHROMOSOMES ALSO ENGAGE IN A  
GOOD DEAL OF **GENE SWAPPING**,  
OR (AS IT'S CALLED) **CROSSING OVER**.

TO ILLUSTRATE, LET'S LOOK  
AT THE EXAMPLE OF THE  
ORDINARY, GARDEN-VARIETY  
TOMATO.



WITH MUTANT  
MAYONNAISE?

...AND TRY NOT TO EAT  
THE EXAMPLE UNTIL  
AFTER CLASS...



TOMATOES HAVE A SKIN-TEXTURE GENE WITH A RECESSIVE ALLELE,  $p$ , WHICH CAUSES HAIRY FRUIT. (OF COURSE, YOU DON'T OFTEN SEE THESE IN THE MARKET!)



LIKewise, THE HEIGHT GENE HAS A RECESSIVE ALLELE,  $d$ , CAUSING DWARF PLANTS.

YOU LIKE IT?

I GIVE IT A  $d$ !



THE RESPECTIVE DOMINANT ALLELES ARE  $p^+$ , WHICH CAUSES SMOOTH FRUIT, AND  $d^+$ , WHICH MAKES TALL PLANTS.

TO TEST THE PRINCIPLE OF INDEPENDENT ASSORTMENT, WE CAN CROSS A DOUBLE RECESSIVE,  $ppdd$ , WITH A HETEROZYGOTE,  $pp^+d^+$ .

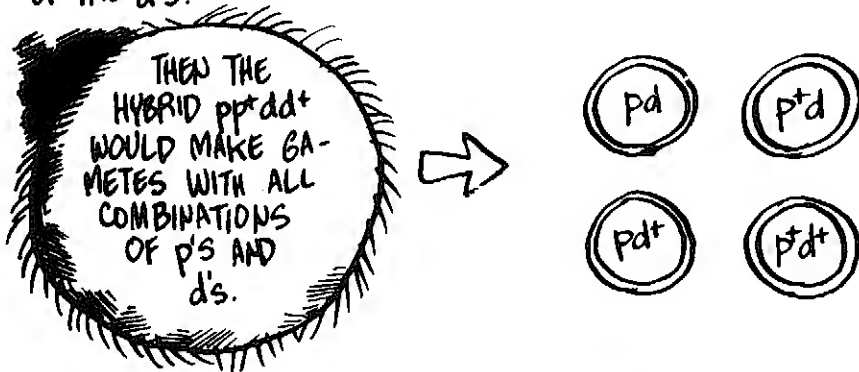


HAIRY, DWARF  
 $ppdd$

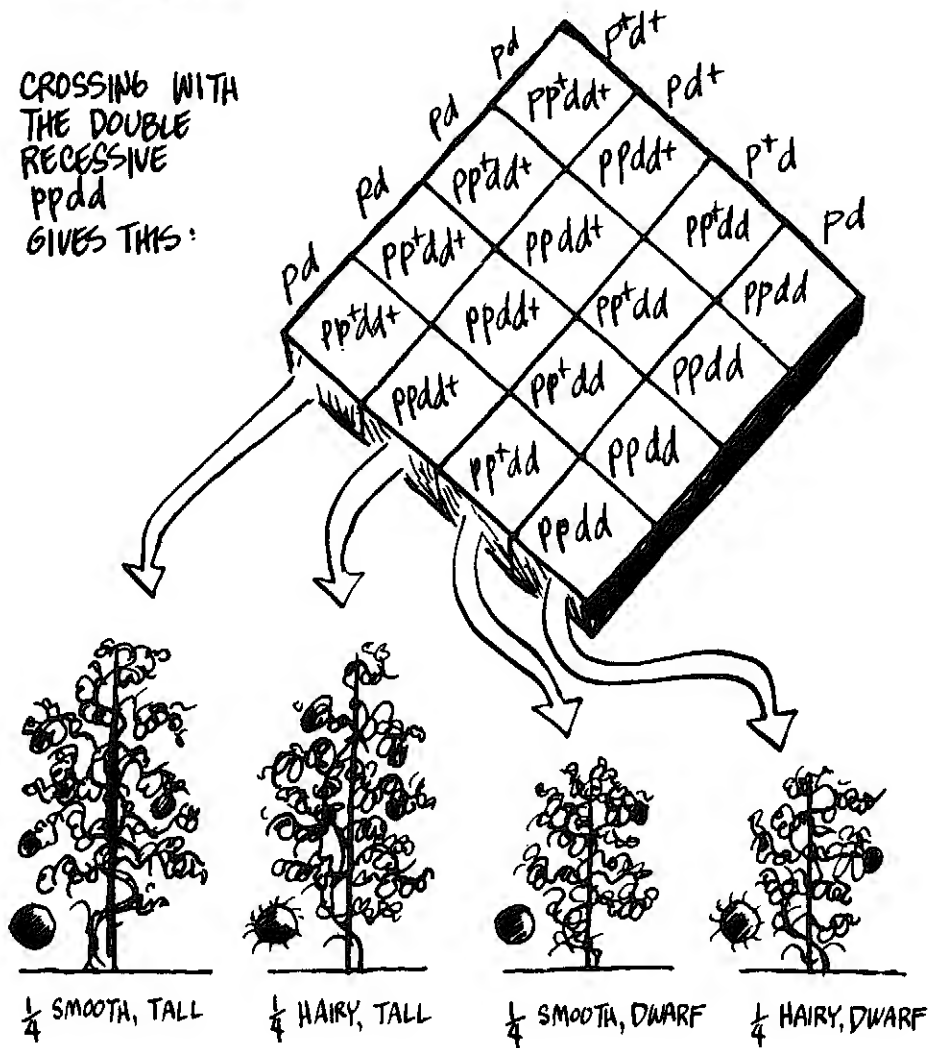


SMOOTH, TALL  
 $pp^+d^+$

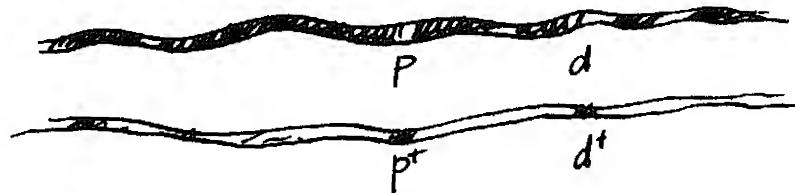
SUPPOSE MENDEL WAS RIGHT, AND THE p's WERE INDEPENDENT OF THE d's.



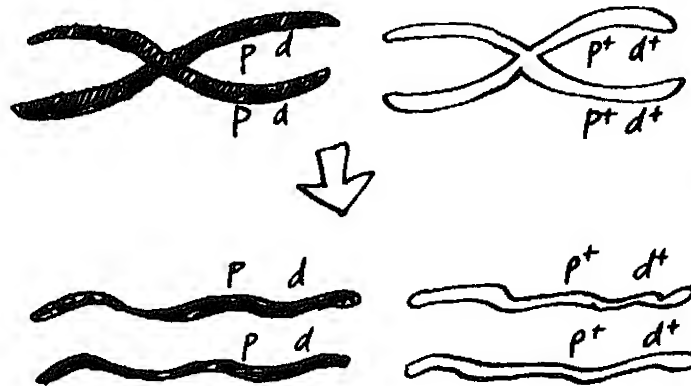
CROSSING WITH THE DOUBLE RECESSIVE  $ppdd$  GIVES THIS:



NOW SUPPOSE P AND d LIE ON THE SAME CHROMOSOME.  
THEN THE HYBRID  $pp^+dd^+$  HAS ITS ALLELES ON A  
HOMOLOGOUS PAIR:



DURING  
MEIOSIS,  
THEY  
ARE  
SORTED  
OUT  
LIKE  
THIS:



IN THIS CASE, ONLY TWO TYPES OF GAMETES CAN BE MADE:  
 $pd$  AND  $p^+d^+$ , RATHER THAN THE FOUR PREDICTED BY MENDEL.

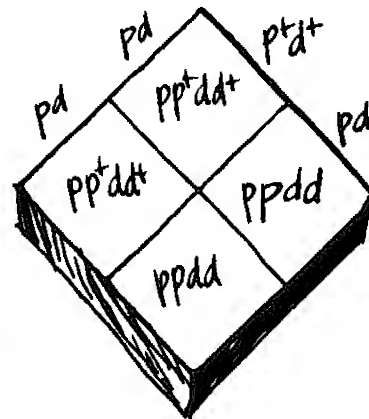
CROSSING WITH THE DOUBLE  
RECESSIVE  $ppdd$ , WE GET



$\frac{1}{2}$  SMOOTH, TALL  
 $pp^+dd^+$



$\frac{1}{2}$  HAIRY, DWARF  
 $ppdd$



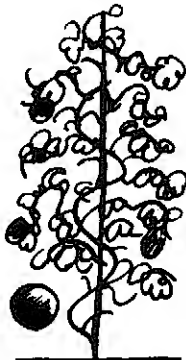
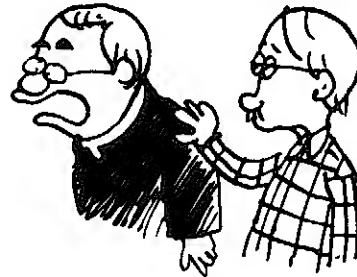


AND OF COURSE,  
WHO'S ON THE  
SIDE OF THE  
ANGELS?

WHEN THE CROSS IS  
ACTUALLY MADE,  
WHAT DOES ONE  
ACTUALLY GET: A 50:50  
SPLIT OR AN EQUAL  
4-WAY SPLIT?

IT SEEMS THAT NEITHER  
PREDICTION IS CORRECT.  
ALL FOUR TYPES DO  
APPEAR, BUT IN THESE  
PROPORTIONS:

SORRY, GREG!



SMOOTH, TALL  
 $Pp^+dd^+$   
48%



HAIRY, TALL  
 $ppdd^+$   
2%



SMOOTH, DWARF  
 $Pp^+dd$   
2%



HAIRY, DWARF  
 $pp\ dd$   
48%

IT'S O.K.,  
I CAN TAKE THE  
DISAPPOINTMENT...

AFTER ALL,  
I AM DEAD -

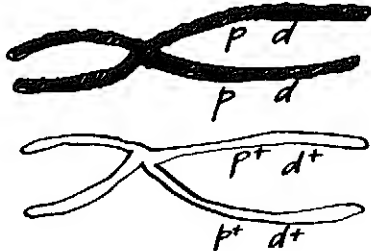
SOB!



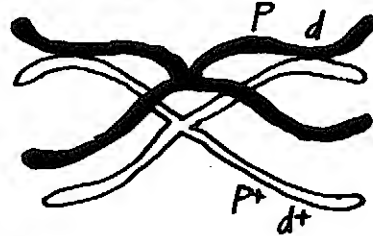
IT'S CERTAINLY  
CLOSER TO THE  
PREDICTION BASED ON  
LINKAGE THAN TO  
MENDEL'S. BUT IF  
P AND d ARE  
LINKED, THEN  
WHERE DID THOSE  
2% COMBINATIONS  
COME FROM??

NOT TO PROLONG THE MYSTERY — THE GENES  $P$  AND  $d$  ARE ON THE SAME CHROMOSOME, BUT CHROMOSOMES CAN EXCHANGE GENES. IT'S CALLED **CROSSING OVER**:

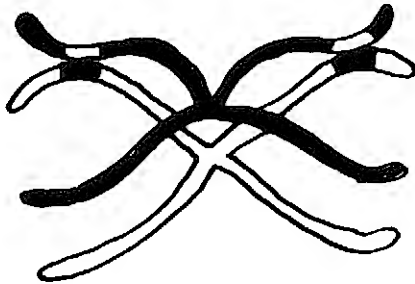
DURING MEIOSIS, HOMOLOGUES LINE UP WITH CORRESPONDING ALLELES OPPOSITE ONE ANOTHER.



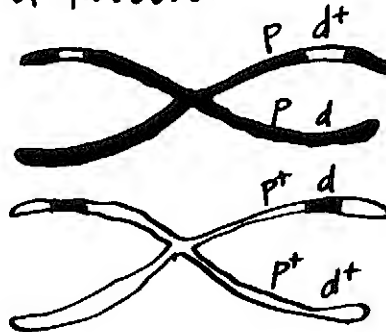
AT CERTAIN POINTS, SEEMINGLY "CHOSEN" AT RANDOM, THE CHROMOSOMES TOUCH:



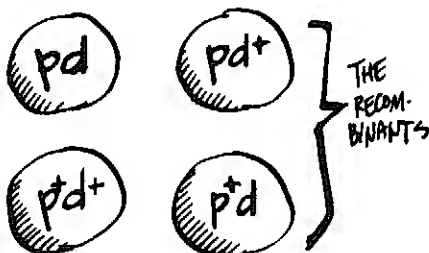
SOME SEGMENTS **CROSS OVER**:



WHEN THEY SEPARATE, THEY HAVE NEW COMBINATIONS OF ALLELES.



WHEN THAT HAPPENS TO OUR HETEROZYGOTE, SOME OF THE RESULTING GAMETES GET THE "RECOMBINANT" CHROMOSOMES. HENCE THE EXCEPTIONAL CROSSES!



NOTE: THANKS TO CROSSING OVER, THE CHROMOSOMES YOU PASS ALONG TO YOUR OFFSPRING ARE NOT EXACTLY YOUR OWN, BUT RATHER A SHUFFLED TOGETHER COMBINATION!

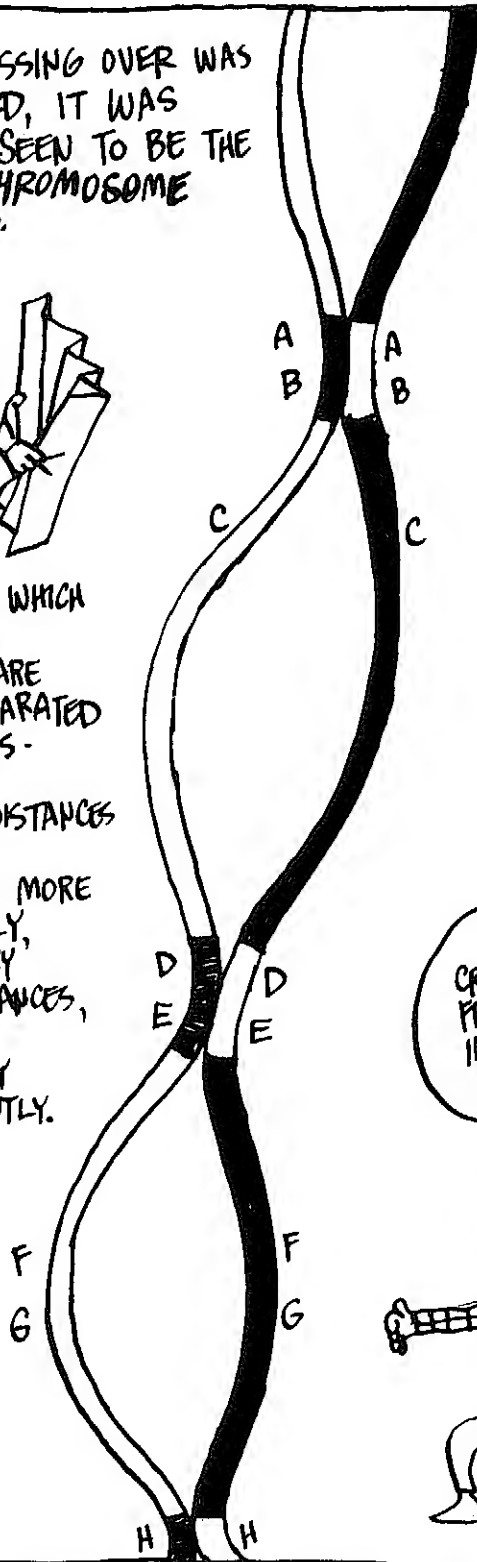


ONCE CROSSING OVER WAS DISCOVERED, IT WAS QUICKLY SEEN TO BE THE KEY TO CHROMOSOME MAPPING.

G.R.D.R.



TWO GENES WHICH ARE CLOSE TOGETHER ARE RARELY SEPARATED BY A CROSS-OVER. AT GREATER DISTANCES THEY ARE SEPARATED MORE FREQUENTLY, AND AT VERY GREAT DISTANCES, THEY ACT COMPLETELY INDEPENDENTLY.



THAT IS, CROSSING OVER FREQUENCY INCREASES WITH DISTANCE!



SO HERE'S HOW YOU MAKE A GENE MAP WITHOUT EVER SEEING A SINGLE GENE:

FIRST, MAKE A VAST NUMBER OF CROSSES BETWEEN INDIVIDUALS DIFFERING IN VARIOUS PAIRS OF TRAITS...

YOU'RE SOME TOMATO!



	A	B	C	D	E	F	G	H
A	0	.27	.03	.04	.33	.48	.19	.41
B	.27	0	.24	.31	.36	.45	.16	.44
C	.03	.24	0	.07	.30			
D	.04	.31	.07	0				
E	.33	.36	.30		0			
F	.48	.45				0		
G	.19	.16					0	
H	.41	.44						0

NEXT, SEE HOW OFTEN EACH PAIR IS SEPARATED BY CROSSING OVER (BY LOOKING AT THE OFFSPRING).

THEN PLOT THEM OUT: THOSE MOST CLOSELY LINKED WILL BE CLOSEST TOGETHER, ETC!

I'VE BEEN MAPPED!

F B D A C G E H

SINCE 1913, MAPPING HAS BEEN APPLIED TO A VARIETY OF ORGANISMS. NEARLY 1000 GENES HAVE BEEN MAPPED IN THE BACTERIUM *E. COLI*; ABOUT 300 IN THE TOMATO; 200 IN THE HOUSE MOUSE...; AND A FEW HUNDRED IN HUMAN BEINGS, ALTHOUGH THIS WAS DONE BY DIFFERENT MEANS...

WHY THE DIFFERENCE FOR HUMANS?

THEY WON'T LET US DO BREEDING EXPERIMENTS..



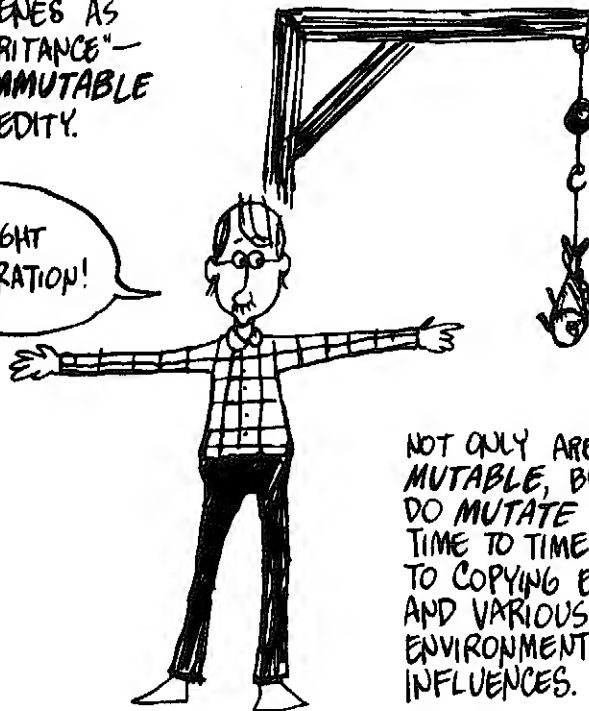
# MUTATION, OR

## A CHANGE OF GENES



SO FAR, WE HAVE BEEN THINKING OF GENES AS "ATOMS OF INHERITANCE"—UNCHANGING, IMMUTABLE UNITS OF HEREDITY.

A SLIGHT EXAGGERATION!



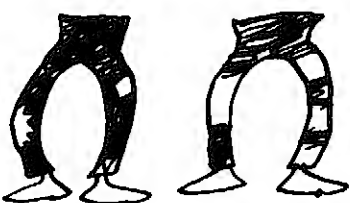
NOT ONLY ARE GENES MUTABLE, BUT THEY DO MUTATE FROM TIME TO TIME, OWING TO COPYING ERRORS AND VARIOUS ENVIRONMENTAL INFLUENCES.



THESE MUTATIONS - IT MEANS "CHANGES" IN LATIN - ARE FAIRLY RARE: THE CHANCE OF FINDING A MUTATION IN A GIVEN GENE IN AN INDIVIDUAL IS

→ 1 IN 100,000


THOUGH SOME GENES ARE MORE PRONE TO CHANGE THAN OTHERS!



EVEN AT THIS RATE, THEY DO ADD UP! A HUMAN HAS SOME 200,000 GENES, SO WE CARRY AN AVERAGE OF TWO NEW MUTATIONS A PIECE.

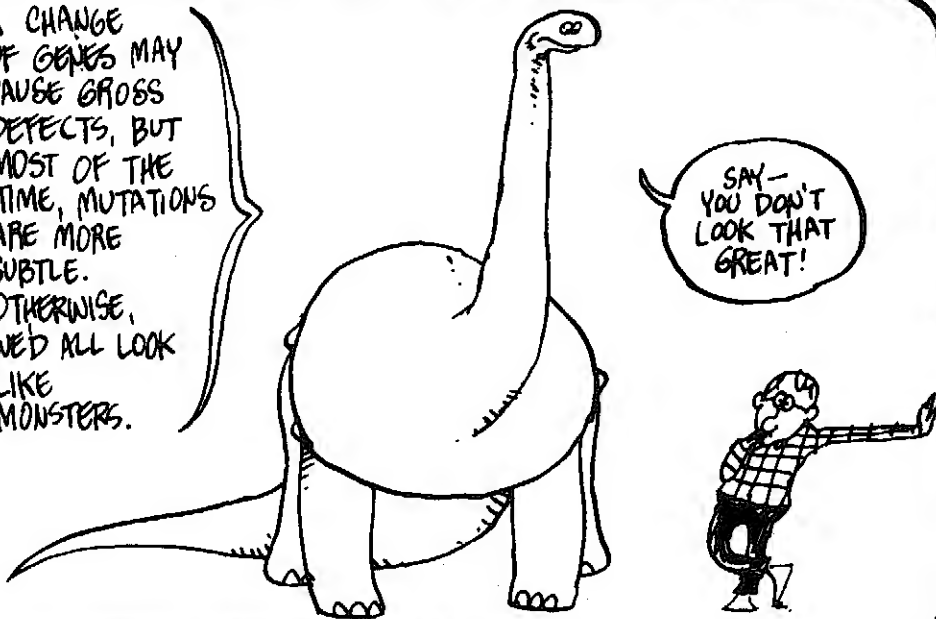
GREAT SHADES!

SORRY... THOSE ARE MY EYES...

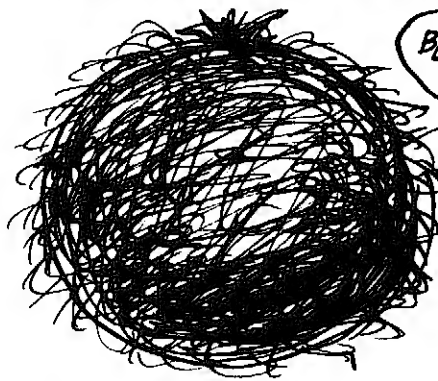


A CHANGE OF GENES MAY CAUSE GROSS DEFECTS, BUT MOST OF THE TIME, MUTATIONS ARE MORE SUBTLE. OTHERWISE, WE'D ALL LOOK LIKE MONSTERS.

SAY - YOU DON'T LOOK THAT GREAT!



SOMETIMES, MUTATIONS  
MERELY RESULT IN  
A NEW **RECESSIVE**  
**ALLELE**, LIKE HAIRINESS  
IN TOMATOES. YOU  
DON'T SEE ANYTHING AT  
ALL UNTIL TWO  
INDIVIDUALS WITH THE  
SAME MUTATION MATE  
TO FORM A **HOMOZYGOTE**.  
THEN

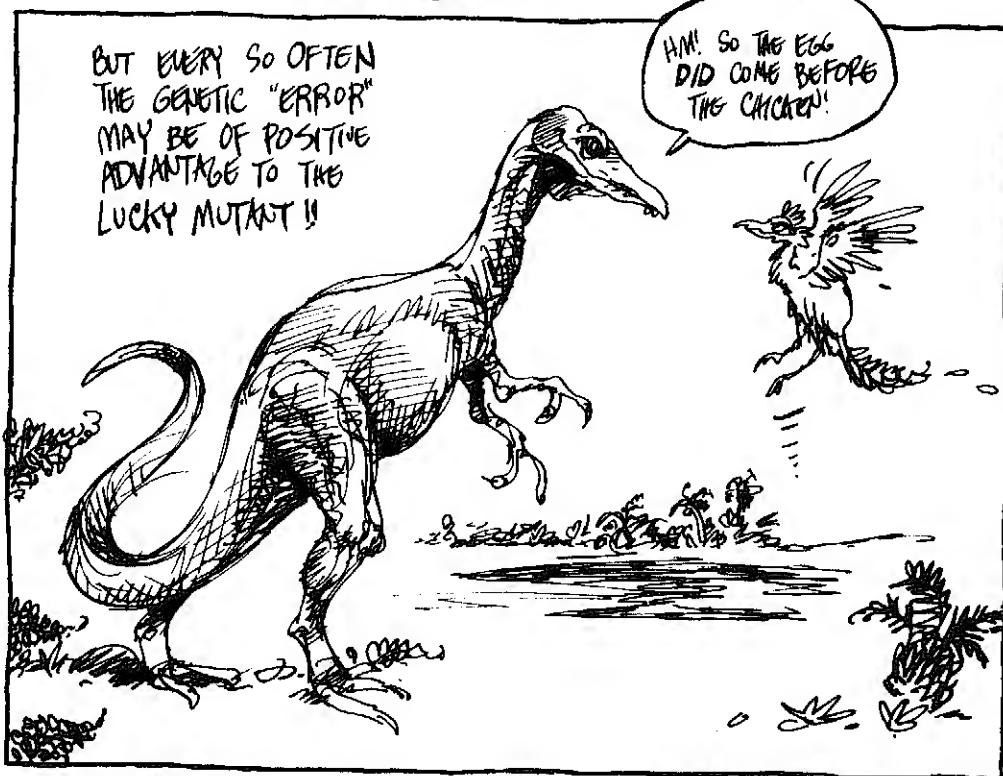


BLEACH!

SOMETIMES MUTATIONS ARE COMPLETELY SILENT — PRODUCING NO  
CHANGE AT ALL — AND SOMETIMES THEY CAUSE CHANGES SO  
SLIGHT AS TO BE BARELY PERCEPTIBLE....

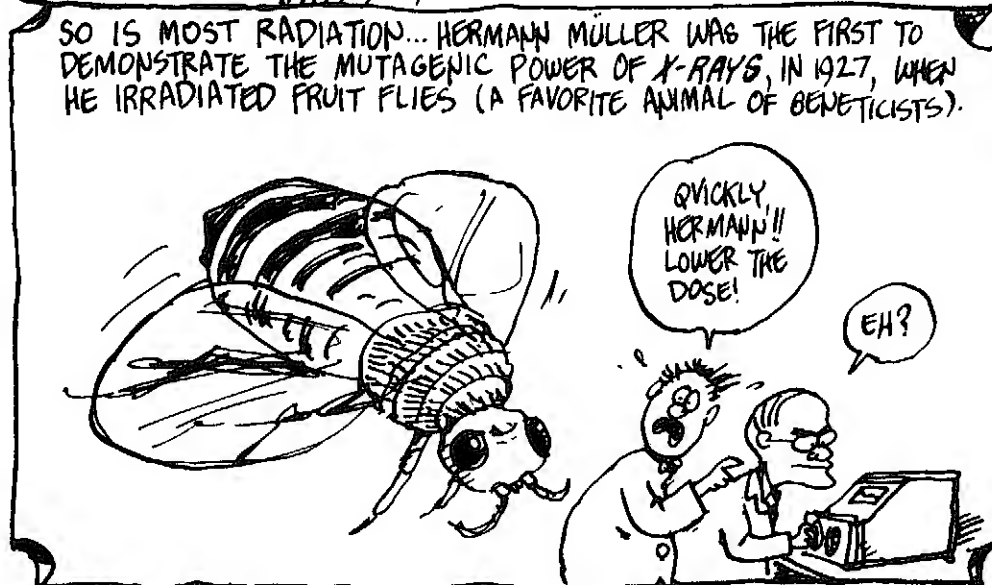
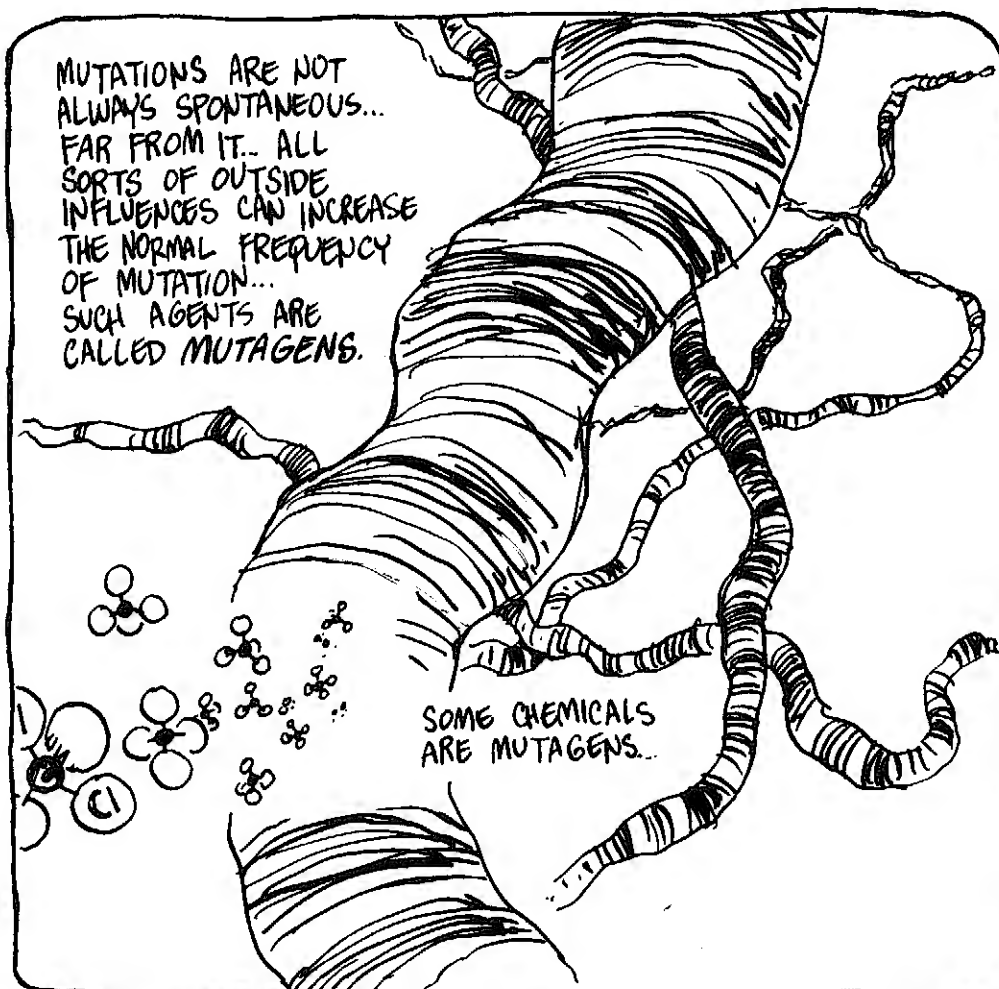


LIKE AN  
EXTRA  
MILLIMETER  
ON THE  
NOSE!



BUT EVERY SO OFTEN  
THE GENETIC "ERROR"  
MAY BE OF POSITIVE  
ADVANTAGE TO THE  
LUCKY MUTANT!!

HMM! SO THE EGG  
DID COME BEFORE  
THE CHICKEN!





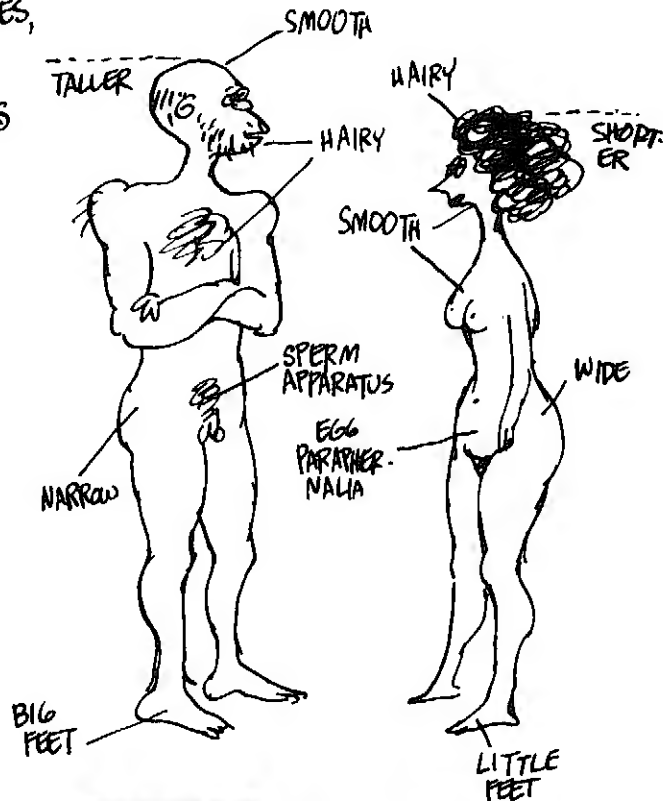
MUTATION IN BODY CELLS (SOMATIC CELLS, AS DISTINCT FROM GERM CELLS) MAY BE INVOLVED IN CANCER... IT MAKES SENSE: THE GENES CONTROL EVERYTHING ABOUT THE CELL, INCLUDING THE PROCESS OF DIVISION. ALTHOUGH THERE ARE STILL MANY MYSTERIES ABOUT CANCER, IT INVOLVES MUTATIONS THAT LEAD THE CELL TO DIVIDE OUT OF CONTROL.

MANY MUTAGENIC AGENTS ARE ALSO CARCINOGENIC (CANCER-CAUSING) — WHICH IS WHY THE FOOD + DRUG PEOPLE LOOK OUT FOR MUTAGENIC FOOD ADDITIVES... AND WHY YOU SHOULD LIMIT YOUR SUNBATHING, ESPECIALLY IF YOU HAVE PALE SKIN. (ULTRAVIOLET LIGHT IS MUTAGENIC.)



# WHAT DETERMINES SEX?

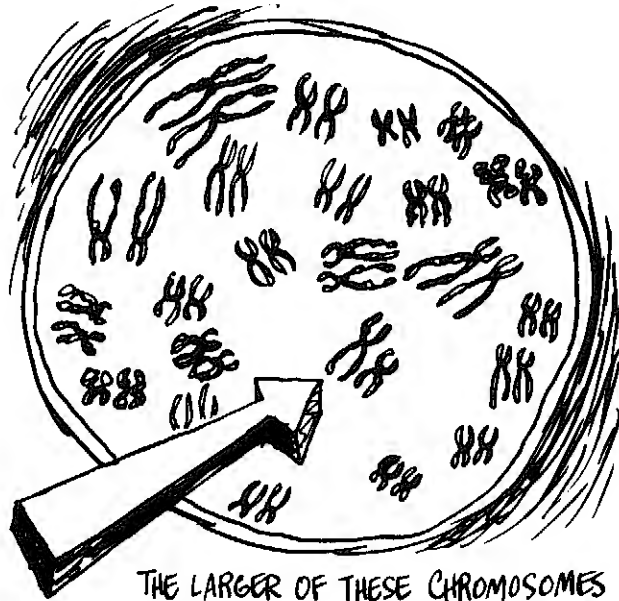
THE COLOR OF PEA FLOWERS, THE TEXTURE OF TOMATOES, THE PINCHING OF PEA PODS—EACH OF THESE QUALITIES IS RULED BY A SINGLE GENE... BUT WHAT GOVERNS THAT MOST OBVIOUS, INTERESTING, AND (IN HUMANS) SUBSTANTIAL DIFFERENCE BETWEEN INDIVIDUALS: THE DIFFERENCE BETWEEN MALE AND FEMALE?



THROUGHOUT HISTORY, SO MANY THINKERS TACKLED THIS QUESTION THAT ONE 18<sup>TH</sup>-CENTURY WRITER WAS INSPIRED TO COMPILE "262 GROUNDLESS HYPOTHESES." HIS OWN GROUNDLESS HYPOTHESIS BECAME THE 263<sup>RD</sup>...



BUT OF COURSE IT'S  
IN THE GENES...  
NOT LONG AFTER  
HOMOLOGOUS  
CHROMOSOMES WERE  
DISCOVERED,  
SOMEBODY NOTICED  
AN EXCEPTION:  
HUMAN MALES HAVE  
ONE PAIR THAT IS  
NOT HOMOLOGOUS!!



THE LARGER OF THESE CHROMOSOMES  
WAS CALLED X; THE SMALLER, Y.

---

THE ONLY GENETIC DIFFERENCE BETWEEN (HUMAN) MALES AND  
FEMALES IS THIS:

FEMALES  
HAVE  
TWO  
X  
CHROMOSOMES:

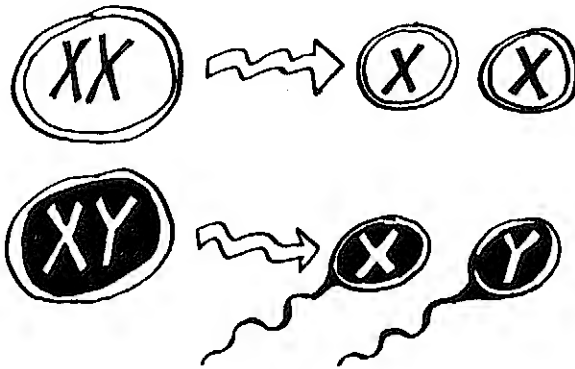


WHILE  
MALES  
HAVE ONE  
X AND  
ONE Y:

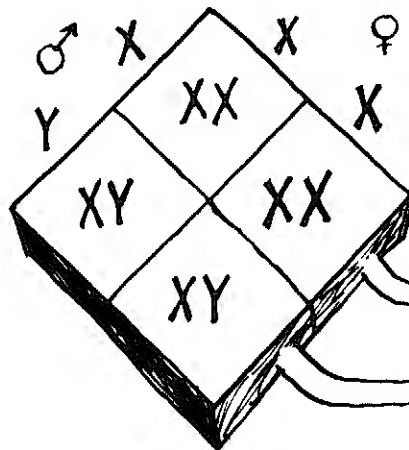


THE OTHER 22 OTHER PAIRS OF CHROMOSOMES ARE THE SAME.

LET'S JUST MAKE  
SURE THIS PRODUCES  
BOY AND GIRL  
BABIES IN THE  
RIGHT AMOUNTS.



MEIOSIS PRODUCES EGGS CARRYING THE X CHROMOSOME; SPERM  
ARE EQUALLY DIVIDED BETWEEN X AND Y—



SO:

$\frac{1}{2}$  GIRLS

$\frac{1}{2}$  BOYS



HOWEVER, THE BASIC GENETIC QUESTION REMAINS: WHICH GENES ARE RESPONSIBLE FOR WHAT? IS IT THE Y CHROMOSOME THAT MAKES A MALE, OR DOES IT TAKE A DOUBLE DOSE OF X TO MAKE A FEMALE? WHAT WOULD HAPPEN TO SOMEBODY WITH TWO X CHROMOSOMES AND A Y ??



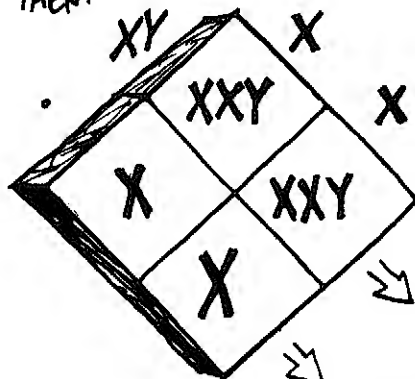
THIS ACTUALLY HAPPENS !!

THESE QUESTIONS ARE ANSWERED BY LOOKING AT CASES OF FAULTY MEIOSIS... SOMETIMES THERE IS AN ERROR IN MAKING SPERM:

NO SEX CHROMOSOME

BOTH SEX CHROMOSOMES

THEN:



THE XXY ("KLINEFELTER'S SYNDROME") GROWS UP MALE. EVEN IN THE PRESENCE OF TWO X CHROMOSOMES, THE Y CAUSES MALENESS. THE SINGLE X GROWS UP FEMALE.

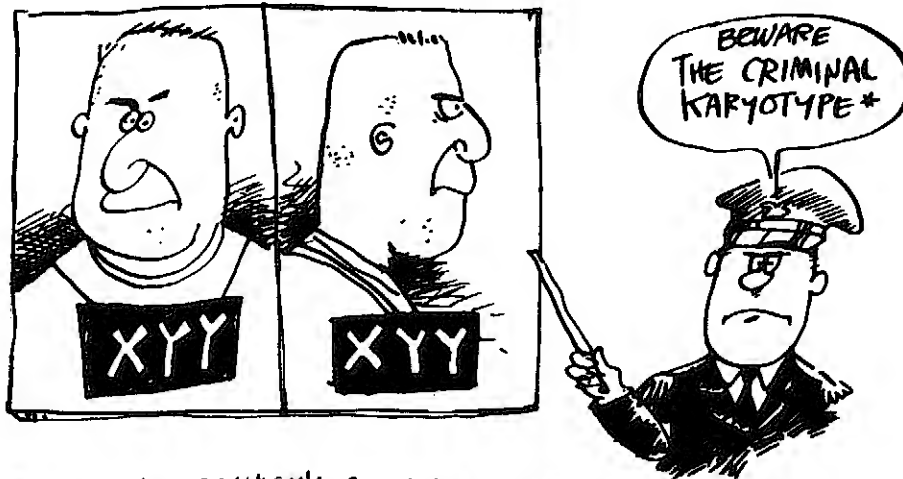
"KLINEFELTER'S SYNDROME"

"TURNER'S SYNDROME"



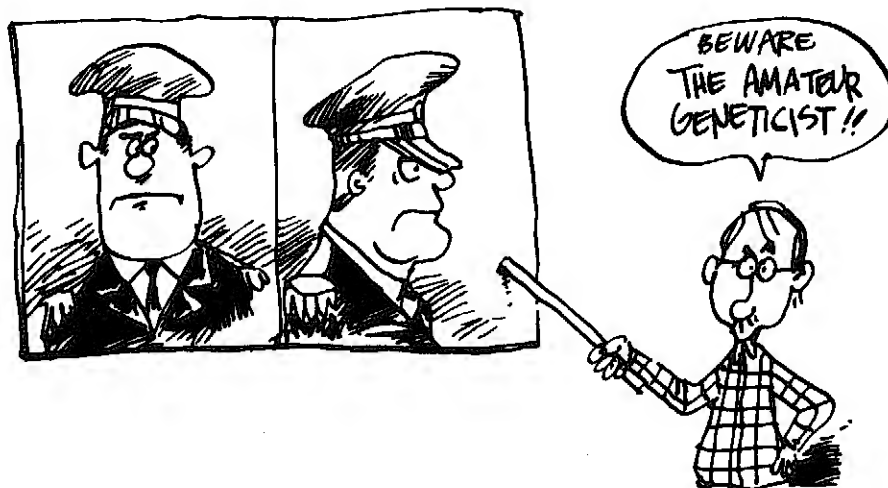


ANOTHER ABNORMALITY IS THE "SUPER MALE" COMBINATION  $XY Y$  WHICH OCCURS IN ABOUT ONE BIRTH IN A THOUSAND.  $XY Y$  CHILDREN GROW UP TO BE NORMAL MALES — EXCEPT THAT THEY END UP IN PRISON ABOUT 20 TIMES MORE OFTEN THAN THE REST OF THE POPULATION. ABOUT 5% OF ALL PRISONERS HAVE AN EXTRA  $Y$  CHROMOSOME. SOME SAY:



\*KARYOTYPE = AN ORGANISM'S PATTERN OF CHROMOSOMES

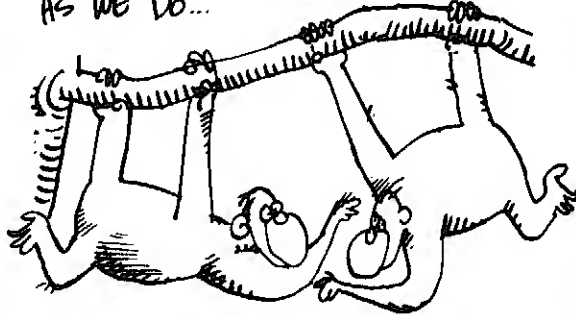
MOST GENETICISTS WOULD BE MORE CAUTIOUS... THE VAST MAJORITY (OVER 95 %) OF  $XY Y$  MALES ARE NOT IN PRISON... SO IT'S IMPOSSIBLE TO SAY THAT THE  $XY Y$  KARYOTYPE CAUSES CRIMINALITY!



DO ANIMALS  
DO IT WITH  
X'S AND Y'S?



NOT NECESSARILY. SEX DETERMINATION IS HANDLED ALL SORTS OF WAYS, THOUGH MANY, MANY SPECIES HAVE THE SAME SYSTEM AS WE DO...



BUT AMONG BIRDS IT'S JUST THE OPPOSITE —



XX =  
MALE

XY = FEMALE

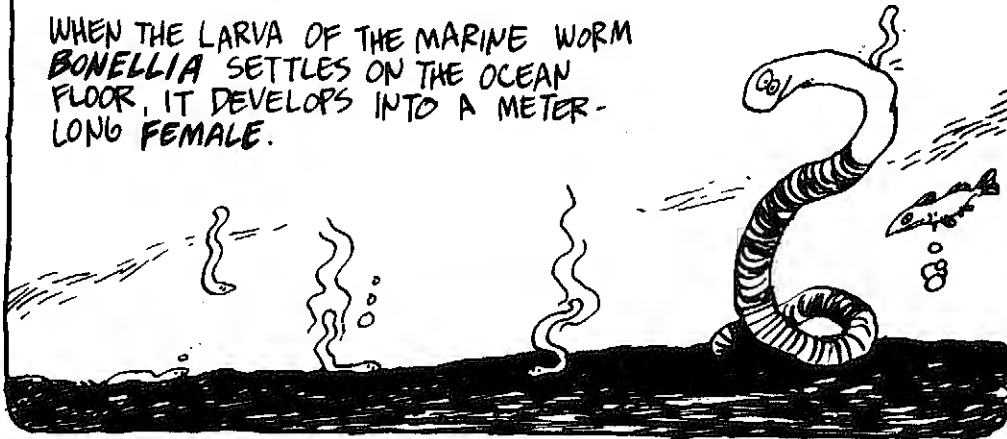
AND BEES ARE REALLY BEE-ZARRE: MALES DEVELOP FROM UNFERTILIZED EGGS. THEY'RE ALL HAPLOID, WHEREAS ALL DIPLOIDS ARE FEMALE (THE VAST MAJORITY OF THE HIVE). OTHERWISE, BEES HAVE NO SPECIFIC SEX CHROMOSOMES.

WILL YOU LISTEN  
TO ME? I SWEAR,  
BUSTER, IT'S LIKE  
YOU'RE ONLY HALF  
THERE SOMETIMES!



THEN THERE ARE THE TRUE ODDITIES, WITH NO GENETIC DIFFERENCE BETWEEN MALE AND FEMALE AT ALL...

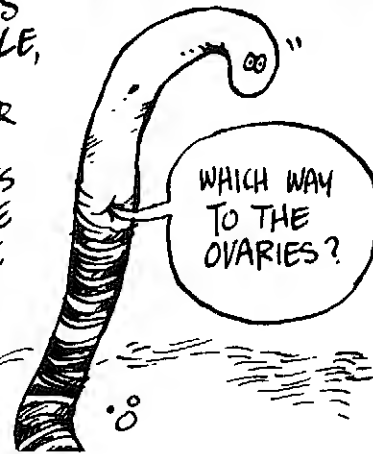
WHEN THE LARVA OF THE MARINE WORM **BONELLIA** SETTLES ON THE OCEAN FLOOR, IT DEVELOPS INTO A METER-LONG FEMALE.



BUT WHEN A LARVA LANDS ON A FEMALE, IT WORMS ITS WAY INTO HER BODY...



...IN WHICH CASE, IT MATURES INTO A MALE, JUST A CENTIMETER LONG, AND PASSES ITS WHOLE LIFE INSIDE THE FEMALE!



AND SOMETIMES SEXUAL DIFFERENCES ARE SIMPLY SUBTLE... CERTAIN PROTOZOA HAVE TWO SEXES, BUT THEY DIFFER ONLY IN A SINGLE GENE... THESE ORGANISMS USUALLY REPRODUCE ASEXUALLY, AS FINDING AN APPROPRIATE PARTNER MUST NOT BE EASY!



EXCUSE ME—ARE YOU ANY DIFFERENT FROM ME?

IF YOU CAN'T TELL, HOW CAN I?



# **X-RATED GENES**

NOW BACK TO HUMANS...  
WE'VE SEEN THAT ALL  
THE GENES ACCOUNTING FOR  
PURELY SEX-RELATED MATTERS  
HAVE ACCUMULATED ON JUST  
TWO CHROMOSOMES, X FOR  
FEMALE, Y FOR MALE...



NOW WE MIGHT ASK THE FOLLOWING

**QUESTION:**

**ARE THERE ANY  
OTHER GENES  
ON THESE CHROMO-  
SOMES ????**

THERE'S A GOOD REASON TO ASK: HUMANS EXHIBIT SEVERAL  
DEFECTS THAT APPEAR TO BE SEX-LINKED...

MOST BALD  
PEOPLE  
ARE MEN.



SO ARE  
MOST  
COLOR-  
BLIND  
PEOPLE.



DITTO  
FOR  
HEMO-  
PHILIACS.\*



\*HEMOPHILIA = A FAILURE OF THE BLOOD TO CLOT. HEMOPHILIACS CAN BLEED TO DEATH FROM A SMALL CUT.

FROM THIS YOU MIGHT CONCLUDE THAT THESE GENES LIE ON THE Y CHROMOSOME — BUT YOU'D BE WRONG!! ACTUALLY, HEMOPHILIA, COLOR-BLINDNESS, AND HEREDITARY BALDNESS ARE ALL CAUSED BY **RECESSIVE** ALLELES LYING ON THE **X** CHROMOSOME!!



TAKE THE EXAMPLE OF BALDNESS:



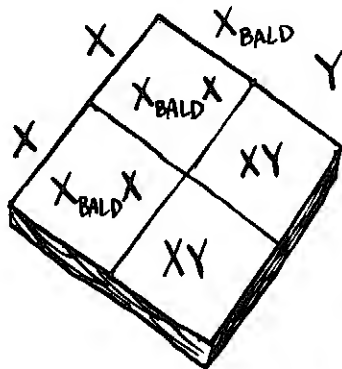
THE REASON WOMEN ARE RARELY BALD IS THAT, EVEN IF THEY HAVE THE BALDNESS ALLELE ON ONE X CHROMOSOME, THEY USUALLY HAVE THE DOMINANT NON-BALD ON THE OTHER.



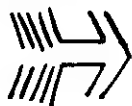
BUT IT SHOWS UP IN MEN BECAUSE THE Y CHROMOSOME HAS NO ALLELE FOR THAT GENE AT ALL. IN THE ABSENCE OF A DOMINANT ALLELE, THE RECESSIVE IS EXPRESSED!!

LET'S SEE HOW THESE SEX-LINKED GENES ARE PASSED ALONG:

SUPPOSE A  
NORMAL WOMAN  
(XX) HAS  
CHILDREN BY  
A BALD MAN  
( $X^{BALD}Y$ ).



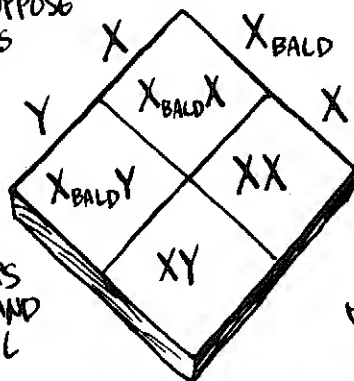
THE DAUGHTERS ( $X^{BALD}X$ )  
ARE ALL CARRIERS.... NOT  
BALD THEMSELVES, THEY STILL  
CARRY THE RECESSIVE GENE.  
THE SONS ARE NORMAL.



IF YOUR MOTHER IS  
NORMAL, YOU CAN'T  
INHERIT BALDNESS  
FROM YOUR FATHER!



NEXT GENERATION: SUPPOSE  
ONE OF THE CARRIERS  
MARRIES A  
NORMAL MAN.



ON THE AVERAGE,  
HALF THE DAUGHTERS  
WILL BE CARRIERS, AND  
HALF THE SONS WILL  
BE BALD!



YOU CAN INHERIT  
BALDNESS FROM  
YOUR MATERNAL  
GRANDFATHER!!



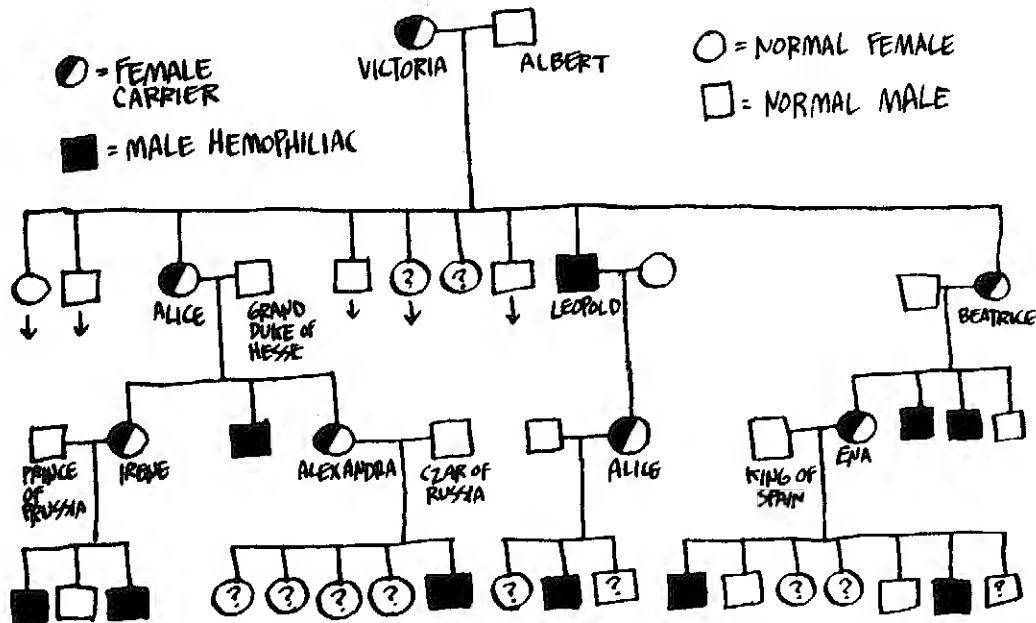


HEMOPHILIA FOLLOWS  
THE SAME PATTERN.  
THE MOST FAMOUS EXAMPLE  
WAS QUEEN VICTORIA  
OF ENGLAND, WHO  
WAS A CARRIER.

THERE IS NO RECORD OF HEMOPHILIA IN VICTORIA'S  
ANCESTORS, SO WE MAY ASSUME THE DEFECT APPEARED  
IN HER GENES AS A SPONTANEOUS MUTATION. THIS HAPPENS  
WITH HEMOPHILIA IN AN ESTIMATED 1 CASE IN EVERY  
50,000 PARENTS.



HEMOPHILIA IS PASSED ALONG JUST LIKE BALDNESS, AND YOU CAN SEE THE PATTERN IN VICTORIA'S FAMILY TREE





WELL,

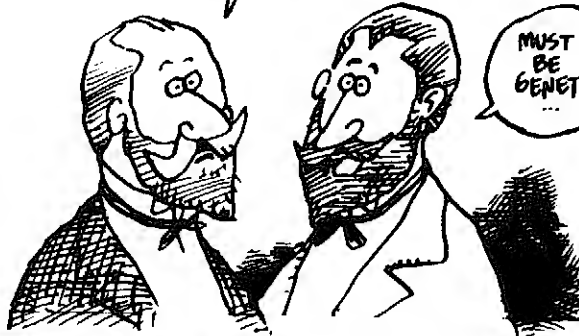
JUST LOOK  
HOW FAR SCIENCE HAD COME  
BY THE EARLY 19<sup>TH</sup> CENTURY:  
MENDEL AND HIS HEIRS  
HAD POLISHED OFF ALL  
THOSE OLD PUZZLES: THE  
ROLE OF MOTHER AND FATHER,  
THE NATURE OF HYBRIDS  
AND "SPORTS," WHAT DETERMINES  
SEX, AND EVEN WHAT CAUSES  
THE QUALITIES OF LIVING  
THINGS...



ALL THESE HAD  
BEEN EXPLAINED  
IN TERMS OF  
**GENES**...  
GENES HAD BEEN  
LOCATED, MAPPED,  
AND THEIR  
PATTERNS OF  
INHERITANCE  
ANALYZED. NOW JUST  
ONE QUESTION  
REMAINED ~.

YES - WHY DO GENETICKISTS  
WEAR POINTED BEARDS??

MUST  
BE  
GENETIC  
...



NO - THE QUESTION IS: WHAT ARE THE GENES, AND HOW DO  
THEY WORK??



GET READY  
TO TRAVEL TO  
UNEXPLORED  
TERRITORY!

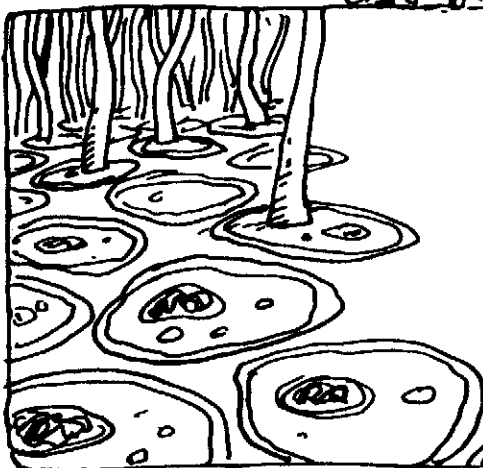
# WHAT'S IN A CELL?

HERE WE SEE A  
COUPLE OF TYPICAL  
LIFE FORMS: A  
GORILLA AND A  
BANANA... THE  
QUESTION IS ~

HOW DO THE **GENES**  
WORK TO MAKE THE  
GORILLA A GORILLA  
AND THE BANANA A  
BANANA...??

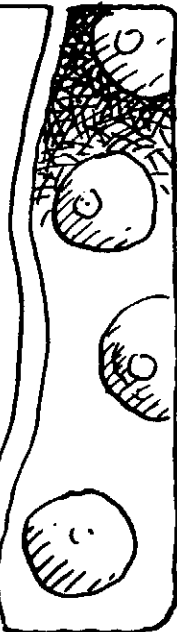


LET'S TAKE  
A CLOSER  
LOOK!



FROM HERE YOU CAN SEE  
HOW THE GORILLA IS  
MADE OF CELLS. TO  
UNDERSTAND THE APE,  
WE'LL HAVE TO MAKE SENSE  
OF WHAT GOES ON IN THESE  
TINY CHEMICAL FACTORIES.

UNFORTUNATELY,  
NOT ALL  
GORILLA  
CELLS ARE  
ALIKE...  
THESE RED  
BLOOD CELLS  
ARE DIFFERENT  
FROM SKIN  
CELLS IN  
SEVERAL  
WAYS..

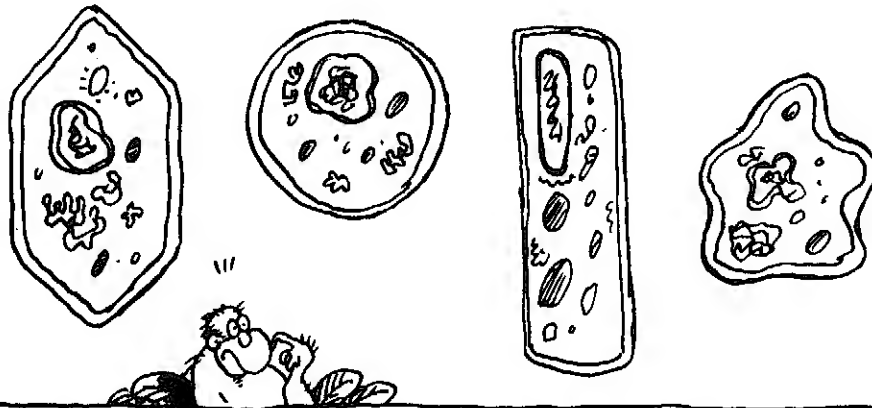


NERVE  
CELLS  
ARE  
LONG  
AND  
SKINNY  
...2→

AND THE  
CELLS  
OF  
MUSCLES,  
EYES,  
KIDNEYS,  
ETC  
ETC  
ETC  
...  
ALL  
DIFFERENT  
!!!



SIMILARLY, THE BANANA PRESENTS A WIDE DIVERSITY OF CELL TYPES...

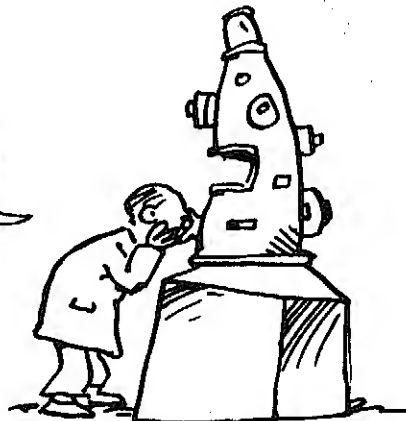


...EACH OF WHICH IS FILLED WITH ALL SORTS OF EVEN TINNER BODIES...



... MAKING BANANAS AND GORILLAS EXTREMELY HARD TO FIGURE OUT !!

HMM... THE GOLGI BODY CONNECTED TO THE ENDOPLASMIC RETICULUM... THE ENDOPLASMIC RETICULUM CONNECTED TO THE NUCLEAR MEMBRANE... NUCLEAR MEMBRANE CONNECTED TO...  
SIGH



WHY DIDN'T I  
LISTEN TO MY MAMA  
AND BECOME A  
LAWYER?

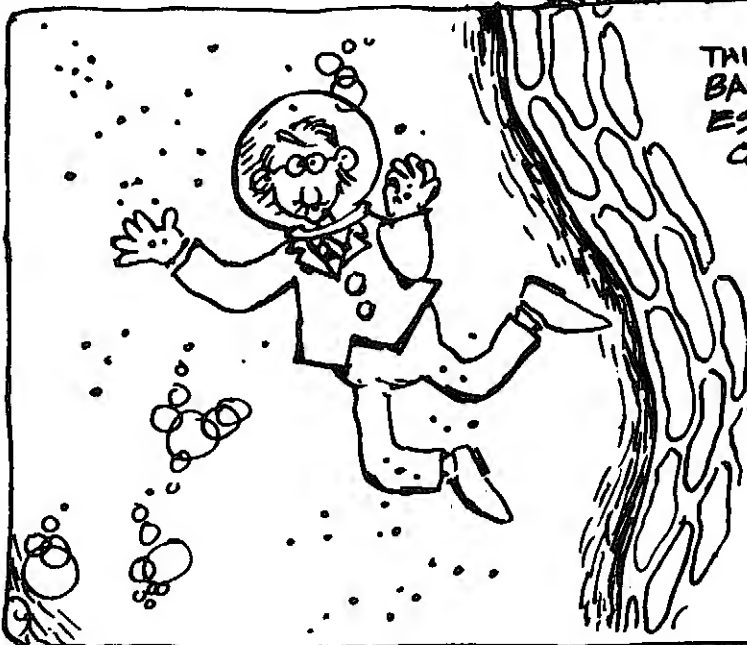


IN FACT, GORILLAS AND  
BANANAS ARE SO  
COMPLICATED, THAT  
FOR MANY YEARS  
SCIENTISTS DESPAIRED  
OF EVER UNDER-  
STANDING THE  
MOLECULAR GENETICS  
OF PLANTS AND  
ANIMALS.

INSTEAD, THEY  
STUDIED A MUCH  
SIMPLER ORGANISM:  
A TINY CREATURE  
FOUND LIVING BY  
THE BILLION —  
RIGHT...IN... HERE!!



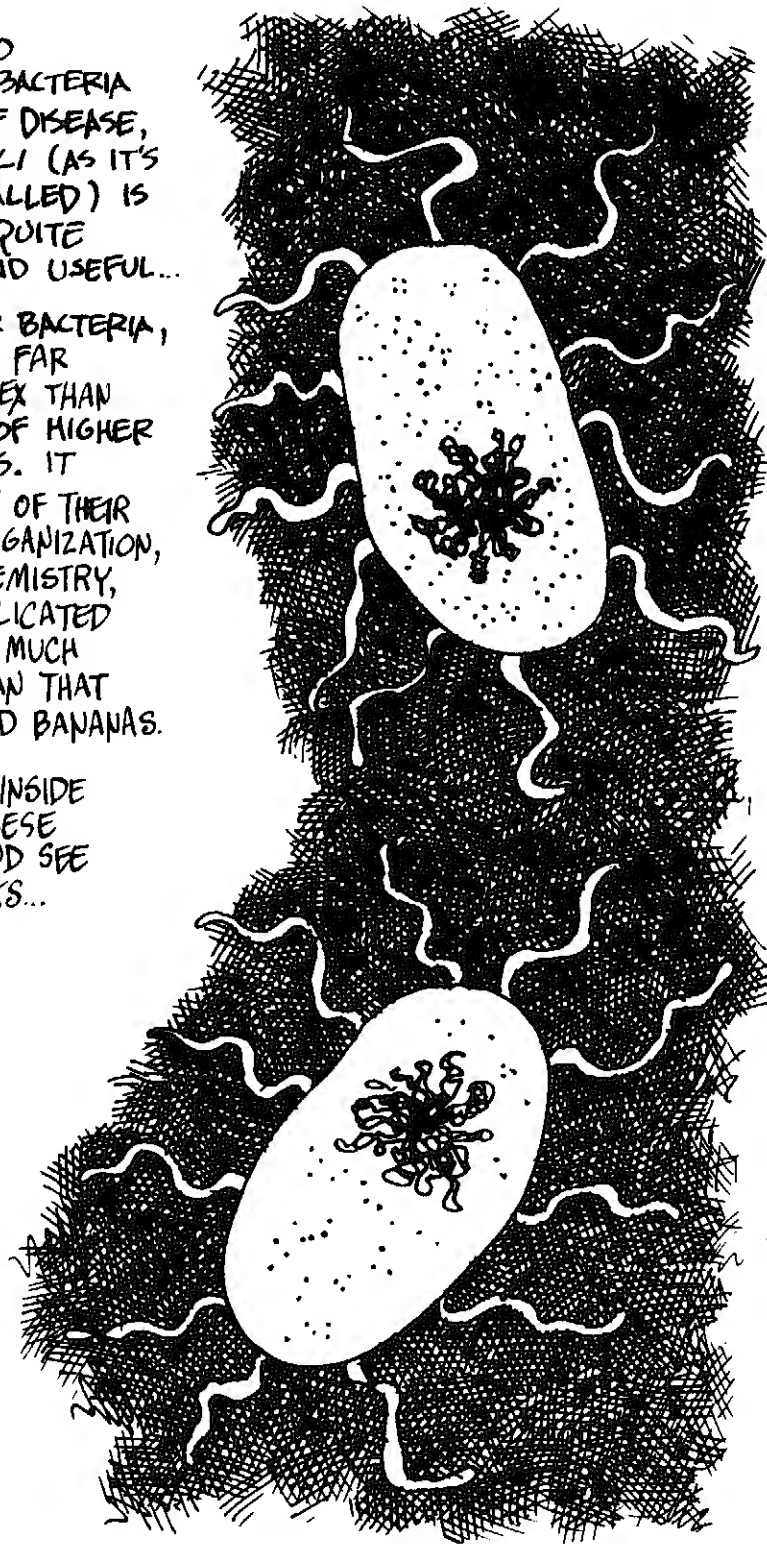
THIS IS THE  
BACTERIUM,  
ESCHERICHIA  
COLI, THAT  
THRIVES IN THE  
INTESTINES OF  
APES AND  
HUMANS.

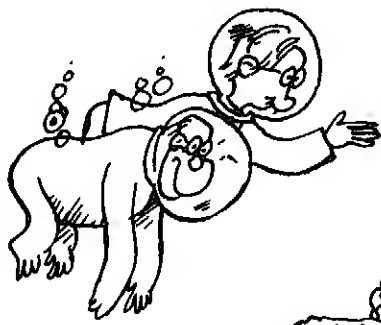


WE TEND TO  
THINK OF BACTERIA  
IN TERMS OF DISEASE,  
BUT *E. COLI* (AS IT'S  
USUALLY CALLED) IS  
ACTUALLY QUITE  
BENIGN AND USEFUL...

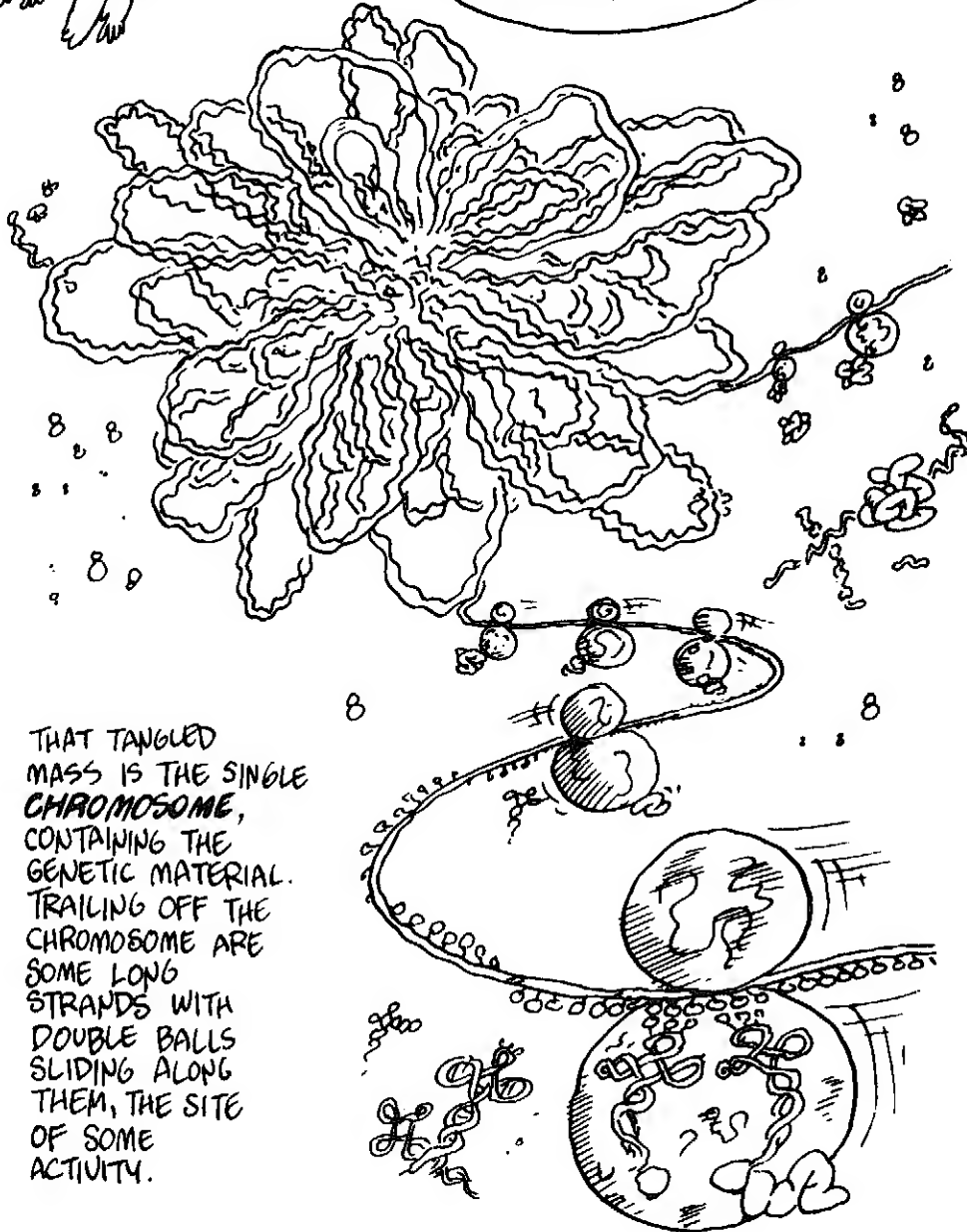
LIKE OTHER BACTERIA,  
*E. COLI* IS FAR  
LESS COMPLEX THAN  
THE CELLS OF HIGHER  
LIFE FORMS. IT  
LACKS MOST OF THEIR  
INTERNAL ORGANIZATION,  
AND ITS CHEMISTRY,  
WHILE COMPLICATED  
ENOUGH, IS MUCH  
SIMPLER THAN THAT  
OF APES AND BANANAS.

LET'S GET INSIDE  
ONE OF THESE  
*E. COLI* AND SEE  
HOW IT LOOKS...

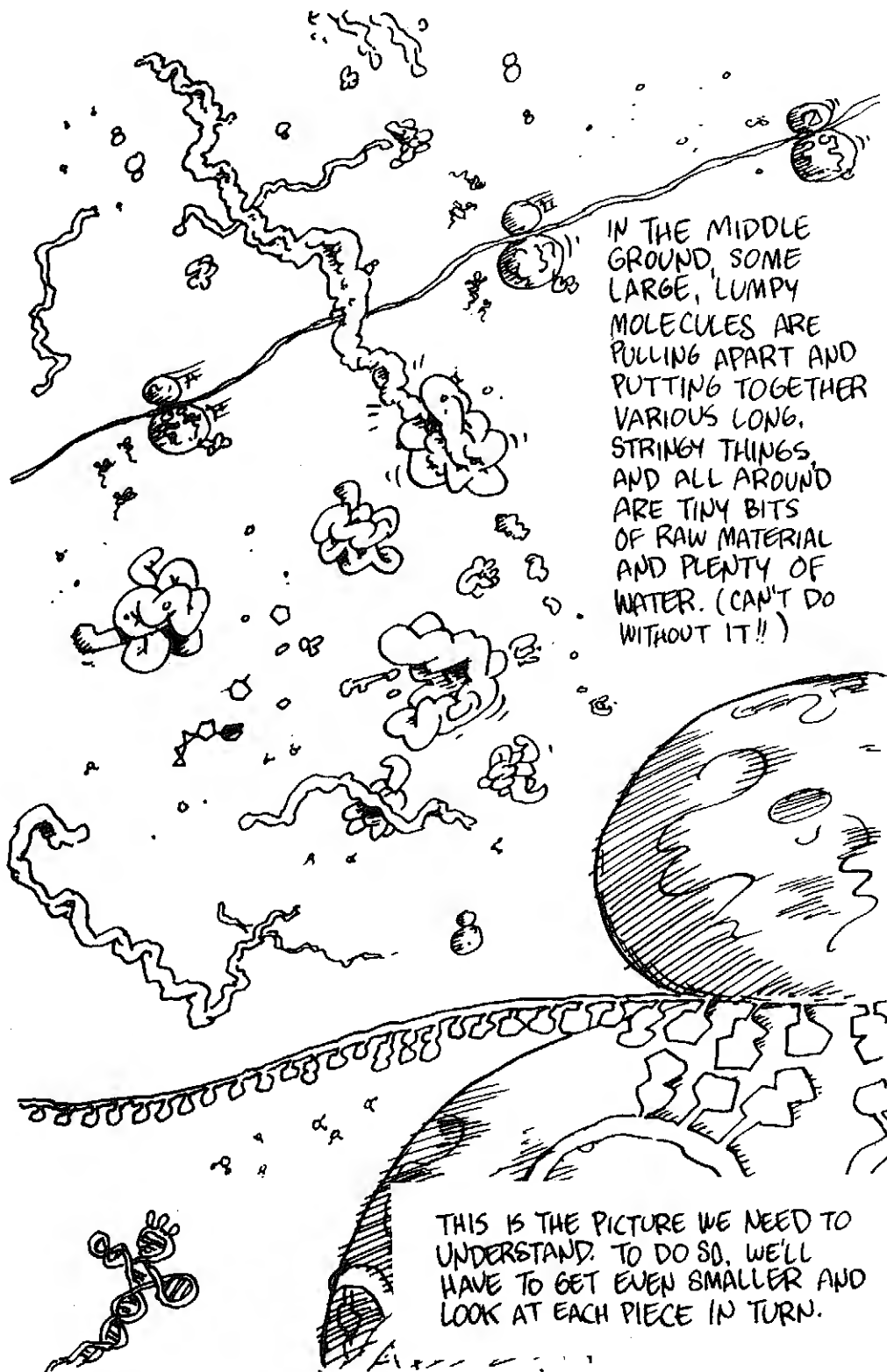




THIS IS THE VIEW  
FROM INSIDE THE BACTERIUM  
*E. COLI* ! ALTHOUGH IT  
LOOKS PRETTY CONFUSING  
AT FIRST, WE CAN MAKE  
OUT A FEW OBVIOUS  
FEATURES!




THAT TANGLED  
MASS IS THE SINGLE  
**CHROMOSOME**,  
CONTAINING THE  
GENETIC MATERIAL.  
TRAILING OFF THE  
CHROMOSOME ARE  
SOME LONG  
STRANDS WITH  
DOUBLE BALLS  
SLIDING ALONG  
THEM, THE SITE  
OF SOME  
ACTIVITY.







# MACROMOLECULES




HYDROGEN



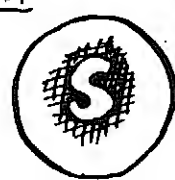
CARBON




NITROGEN



OXYGEN



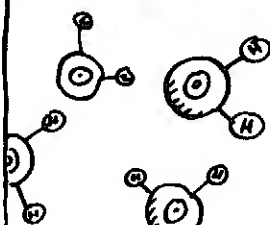
SULFUR



PHOSPHORUS

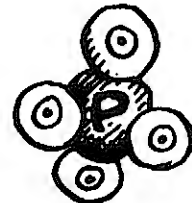
SURPRISING AS IT MAY SEEM,  
ALMOST EVERYTHING IN THAT  
COMPLEX PICTURE IS MADE OF  
JUST SIX DIFFERENT ELEMENTS.

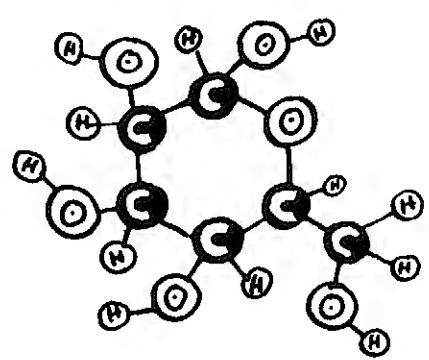
IN THE CELL THESE ATOMS ARE JOINED TOGETHER TO  
FORM **MOLECULES**.



THE SIMPLEST AND MOST  
ABUNDANT BY FAR IS  
**WATER**,  $H_2O$ .

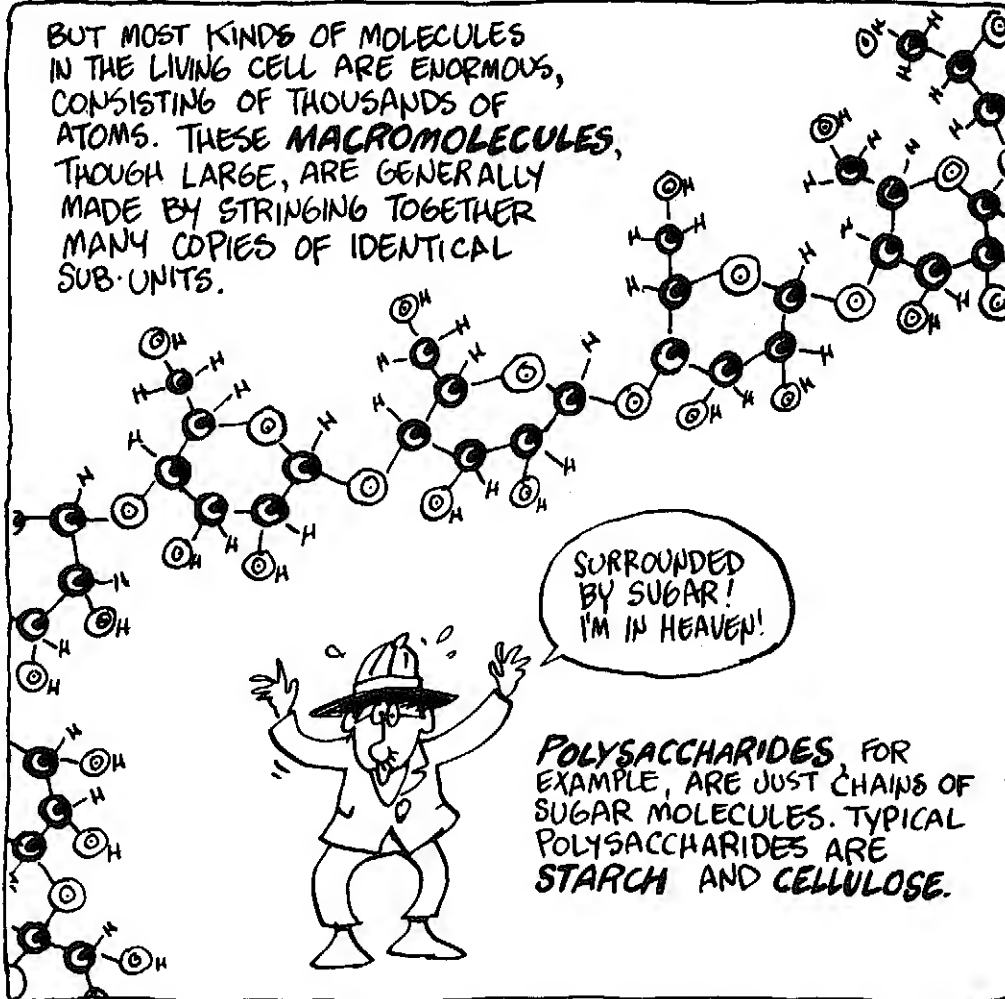
ANOTHER SMALL ONE IS  
THE PYRAMID-SHAPED  
**PHOSPHATE**,  $PO_4$ .



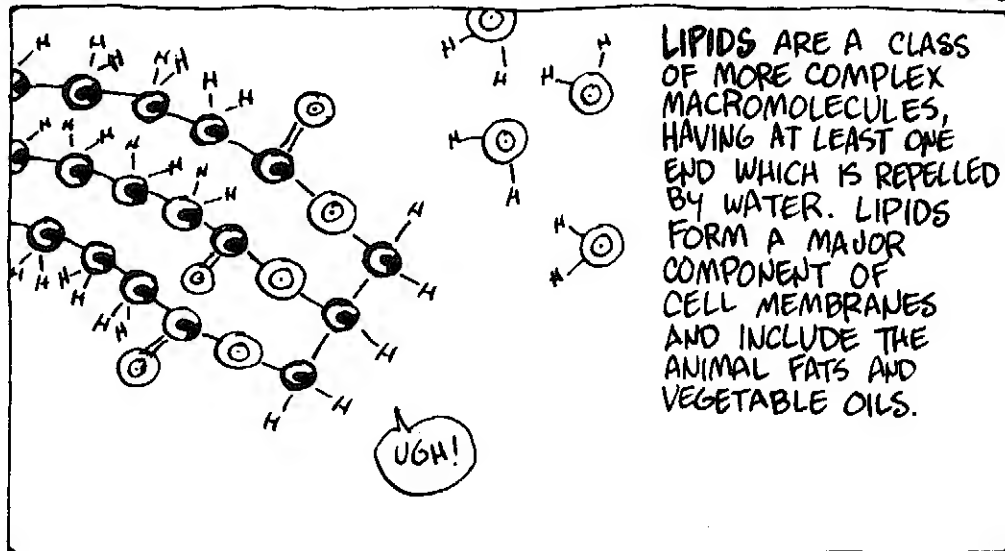


A BIT BIGGER ARE  
THE RING-SHAPED  
**SUGARS**. THIS ONE  
IS **GLUCOSE**,  $C_6H_{12}O_6$ .

BUT MOST KINDS OF MOLECULES IN THE LIVING CELL ARE ENORMOUS, CONSISTING OF THOUSANDS OF ATOMS. THESE **MACROMOLECULES**, THOUGH LARGE, ARE GENERALLY MADE BY STRINGING TOGETHER MANY COPIES OF IDENTICAL SUB-UNITS.



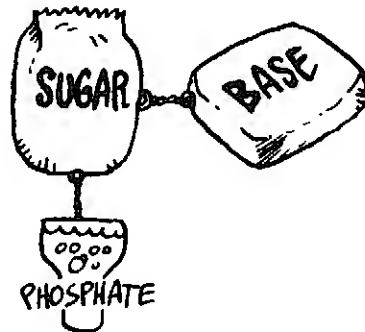
**POLYSACCHARIDES**, FOR EXAMPLE, ARE JUST CHAINS OF SUGAR MOLECULES. TYPICAL POLYSACCHARIDES ARE **STARCH** AND **CELLULOSE**.



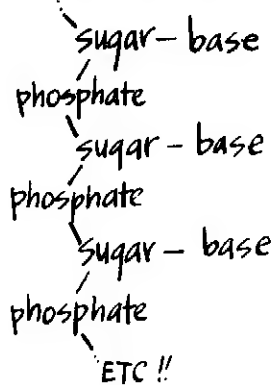
**LIPIDS** ARE A CLASS OF MORE COMPLEX MACROMOLECULES, HAVING AT LEAST ONE END WHICH IS REPELLED BY WATER. LIPIDS FORM A MAJOR COMPONENT OF CELL MEMBRANES AND INCLUDE THE ANIMAL FATS AND VEGETABLE OILS.

**S**TILL MORE COMPLEX, BUT MOST IMPORTANT IN GENETICS, ARE THE **NUCLEIC ACIDS** AND **PROTEINS**... WATCH CLOSELY:

THE BUILDING BLOCKS FOR NUCLEIC ACIDS ARE CALLED **NUCLEOTIDES**. AN INDIVIDUAL NUCLEOTIDE ITSELF HAS 3 COMPONENTS: A **SUGAR**, A **PHOSPHATE**, AND A **BASE**, LIKE SO —

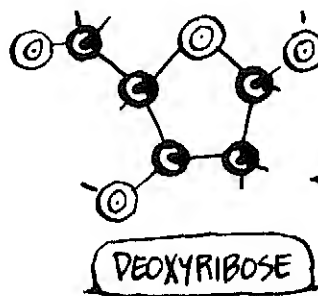
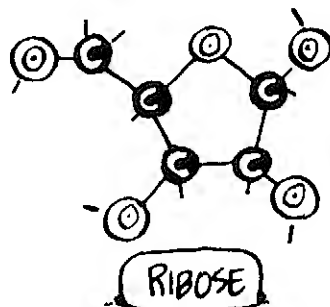


THESE ARE HOOKED TOGETHER TO MAKE A LONGGGGGG SUGAR-PHOSPHATE "BACKBONE" WITH A SEQUENCE OF BASES STICKING OFF:



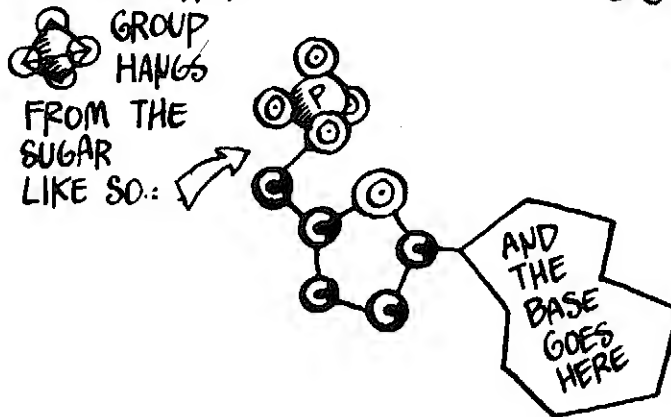
THIS MAY GO ON FOR MILLIONS OF NUCLEOTIDES!

THE SUGAR MAY BE ONE OF TWO KINDS, WHICH WE ILLUSTRATE HERE WITHOUT ALL THEIR PESKY HYDROGEN ATOMS. (THEY JUST CLUTTER UP THE PICTURE!)



← YOU SEE? ONE LESS OXYGEN!

THE PHOSPHATE  
GROUP  
HANGS  
FROM THE  
SUGAR  
LIKE SO.:

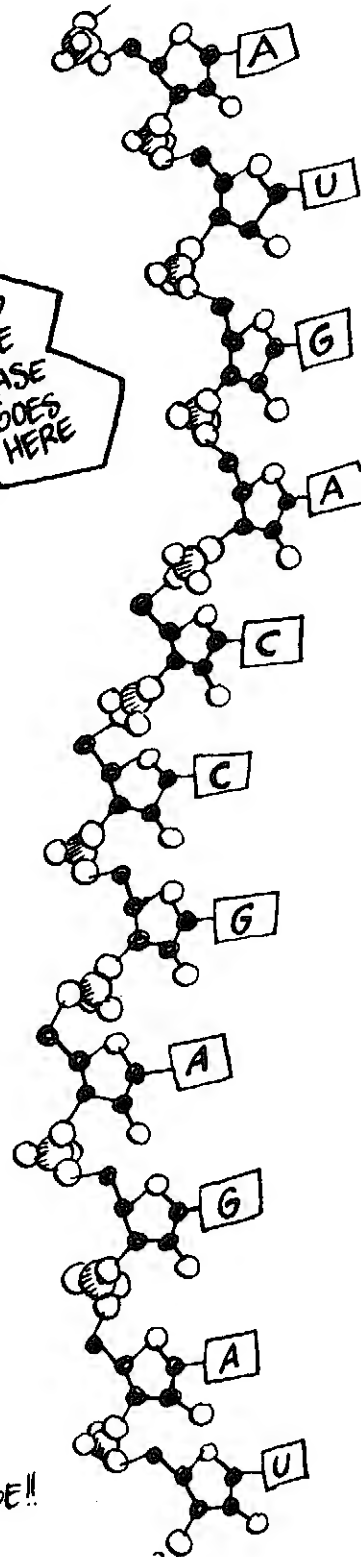


WE'LL TOUCH THE BASES  
LATER ..... FOR NOW  
WE'LL JUST SAY THERE  
ARE 5 KINDS, WITH THE  
NICKNAMES A, C, G, T,  
AND U.

IN ANY GIVEN NUCLEIC  
ACID MACROMOLECULE,  
ALL THE SUGARS ARE  
THE SAME.

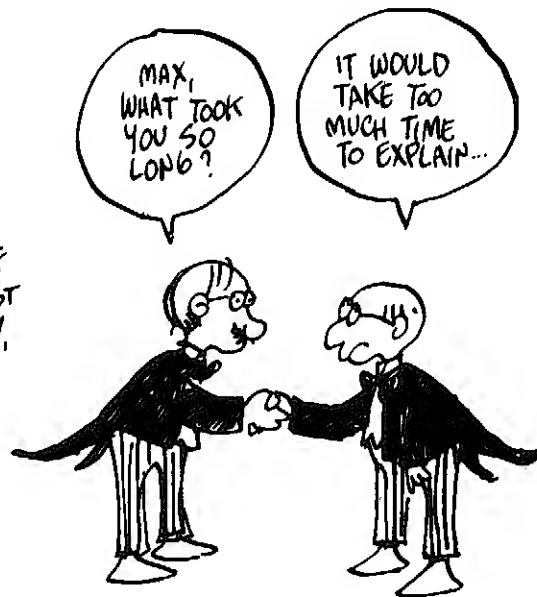
➡ NUCLEIC ACIDS WITH  
RIBOSE ARE CALLED  
RIBONUCLEIC ACID,  
OR RNA. THOSE WITH  
DEOXYRIBOSE ARE  
CALLED DNA (DEOXY-  
RIBONUCLEIC ACID, OF  
COURSE!).

IN BOTH DNA AND RNA,  
THE BASES MAY BE DIFFERENT  
FROM ONE NUCLEOTIDE TO  
THE NEXT, GIVING NUCLEIC ACIDS  
THE APPEARANCE OF MESSAGES  
IN SOME STRANGE MOLECULAR LANGUAGE!!



# PROTEINS

ARE THE MOST COMPLICATED MACROMOLECULES OF ALL. THE BIOLOGIST MAX PERUTZ SPENT 25 YEARS - MOST OF HIS CAREER - ANALYZING JUST ONE OF THEM: HEMOGLOBIN, THE PROTEIN THAT CARRIES OXYGEN THROUGH THE BLOODSTREAM. FOR THIS, PERUTZ RECEIVED THE NOBEL PRIZE IN 1962...



YET IN A CERTAIN SENSE, PROTEINS ARE SIMPLE, TOO: LIKE OTHER MACROMOLECULES, THEY ARE LONG CHAINS OF SMALLER SUBUNITS.



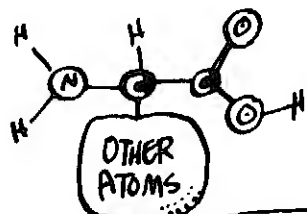
ACTUALLY, HEMOGLOBIN IS TWO PAIR OF SUCH CHAINS, WRAPPED UP IN A SYMMETRICAL TANGLE.

THE SUBUNITS OF PROTEIN MOLECULES ARE AMINO ACIDS, WHICH ARE NOT NAMED AFTER IDI AMIN, THE FORMER DICTATOR OF UGANDA.



OH! O.K...

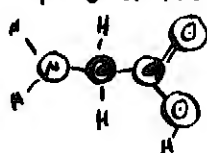
THE TYPICAL AMINO ACID  
LOOKS LIKE THIS:



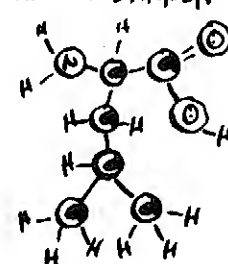
IT'S THAT CLUSTER OF  
"OTHER ATOMS" THAT  
COMPLICATES MATTERS...



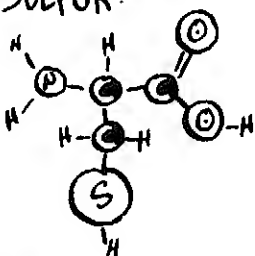
GLYCINE IS  
QUITE SIMPLE:



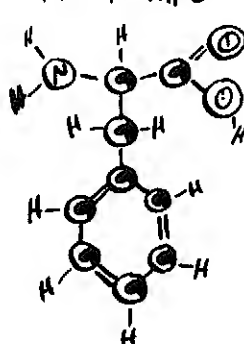
LEUCINE  
HAS A BRANCH:



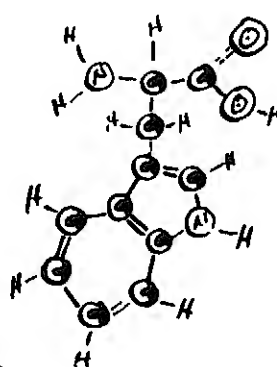
CYSTEINE CONTAINS  
SULFUR:



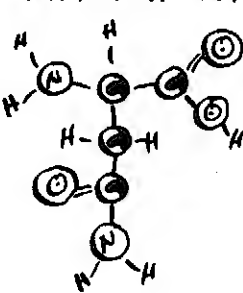
PHENYLALANINE  
HAS A RING:



TRYPTOPHAN  
HAS RINGS ON  
RINGS:



ASPARAGINE HAS  
EXTRA NITROGEN:

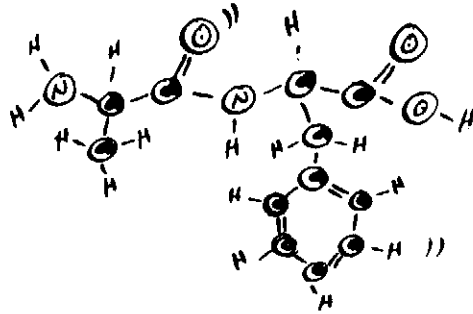


SO WERE  
THE CHEMISTS!  
HA HA HA HA

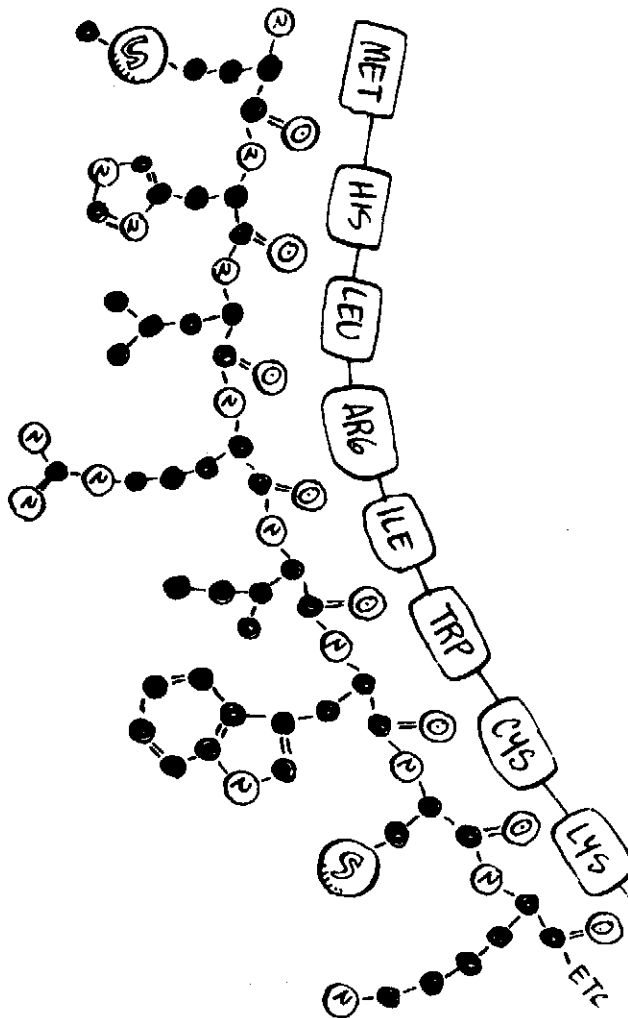
IN ALL, SOME 20  
"STANDARD" AMINO  
ACIDS GO INTO  
PROTEINS:

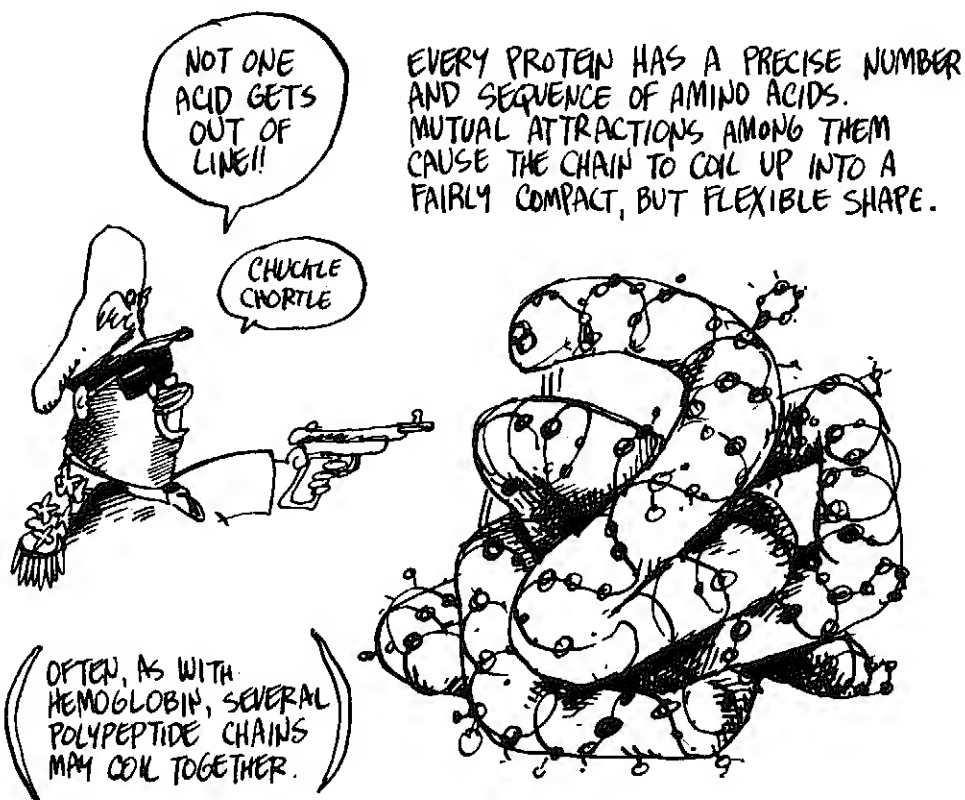
AMINO ACID	ABBREVIATED AS:
GLYCINE	GLY
ALANINE	ALA
VALINE	VAL
LEUCINE	LEU
ISOLEUCINE	ILE
SERINE	SER
THREONINE	THR
ASPARTIC ACID	ASP
GLUTAMIC ACID	GLU
LYSINE	LYS
ARGININE	ARG
ASPARAGINE	ASN
GLUTAMINE	GLN
CYSTEINE	CYS
METHIONINE	MET
PHENYLALANINE	PHE
TYROSINE	TYR
TRYPTOPHAN	TRP
HISTIDINE	HIS
PROLINE	PRO

(HYDROGENS OMITTED!)



ANY TWO OF THEM CAN JOIN TOGETHER  
TO FORM A **PEPTIDE**...VERY PEPPY...  
ADD SOME MORE AND YOU GET A  
**POLYPEPTIDE**, OR **PROTEIN**  
**CHAIN**...





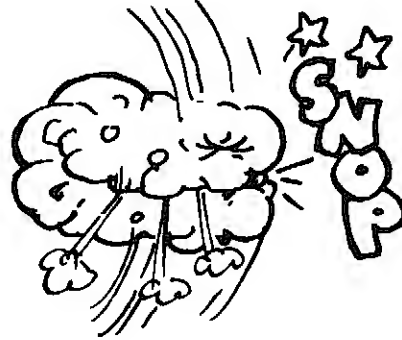


ENZYMES ARE PROTEINS WHICH TAKE APART OR PUT TOGETHER OTHER MOLECULES. EACH ENZYME IS RESPONSIBLE FOR JUST ONE SPECIFIC REACTION.

A TYPICAL ENZYME LIES IN WAIT FOR THE RIGHT MOLECULES TO COME AROUND.



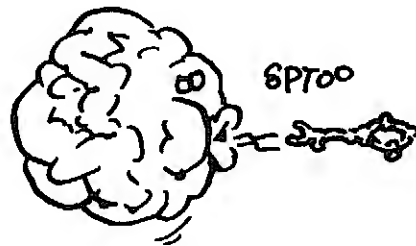
THE ENZYME BINDS TO THE SMALL MOLECULES...



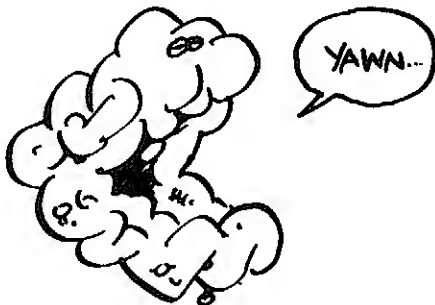
...AND COMBINES THEM...



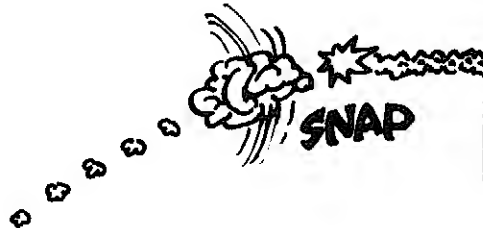
...INTO A NEW MOLECULE, WHICH IS RELEASED.



THE ENZYME ITSELF REMAINS UNCHANGED IN THE PROCESS.

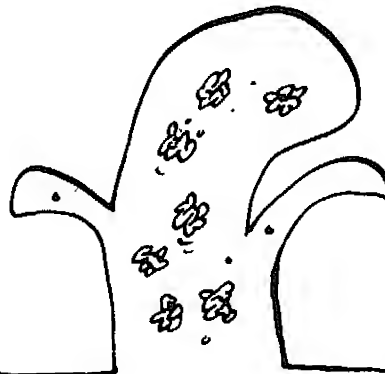


IN A SIMILAR WAY, **DIGESTIVE** ENZYMES BREAK DOWN LARGE MOLECULES. SEVERAL KINDS, FOR EXAMPLE, CHOP SUGARS OFF POLYSACCHARIDES !!



THESE PROTEINS ARE SO IMPORTANT BECAUSE VIRTUALLY EVERY ONE OF LIFE'S CHEMICAL REACTIONS IS DRIVEN BY SOME ENZYME.

WHEN CHEMICALS COME UP THROUGH THE ROOTS OF THE BANANA TREE, THE PLANT'S ENZYMES CONVERT THEM INTO THE CONSTITUENTS OF A BANANA...



THEN, WHEN THE GORILLA EATS THE BANANA, THE APE'S ENZYMES DIGEST THE FRUIT AND TURN IT INTO AN APE...

...AND LIKEWISE FOR E. COLI, WHICH HAS ITS OWN ENZYMES...!

IN OTHER WORDS:

An organism  
is made by  
its enzymes.

AND WHAT  
DO YOU SUP-  
POSE MAKES  
THE ENZYMES?

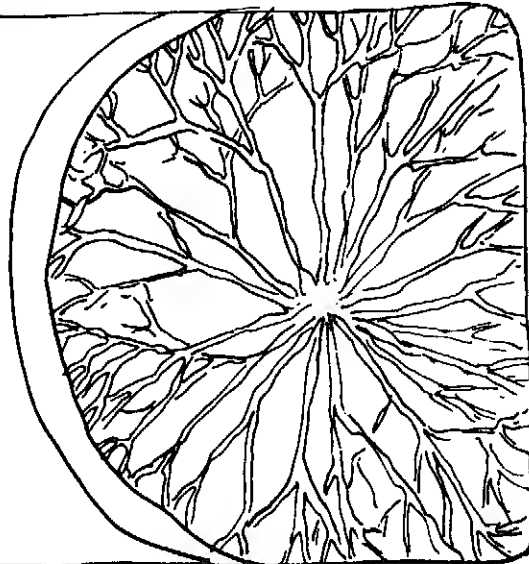


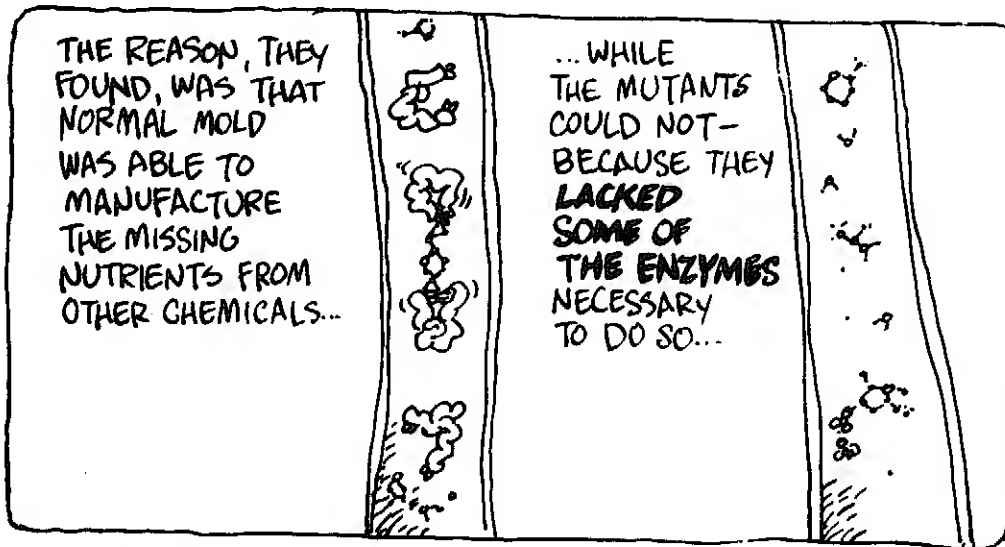
# ONE GENE, ONE ENZYME



THE RELATIONSHIP BETWEEN GENES AND ENZYMES FIRST BECAME CLEAR IN THE 1940'S, THANKS TO EXPERIMENTS PERFORMED BY BIOLOGISTS **GEORGE BEADLE** AND **EDWARD TATUM**, WORKING WITH MUTANT STRAINS OF THE COMMON BREAD MOLD **NEUROSPORA** GROWN IN BATHS OF CHEMICAL NUTRIENTS.

EACH MUTANT WAS FOUND TO REQUIRE **MORE CHEMICAL NUTRIENTS** IN ITS DIET THAN WERE NEEDED BY NORMAL MOLD. FOR EXAMPLE, ONE MUTANT HAD TO BE FED AN EXTRA AMINO ACID, WHILE ANOTHER REQUIRED A CERTAIN VITAMIN.





BY EXHAUSTIVE CROSS-BREEDING AND BIOCHEMICAL ANALYSIS, THE SCIENTISTS DISCOVERED THIS: **THE MUTATION OF A SINGLE GENE LED TO THE LACK OF A SINGLE ENZYME...**



\*\*\*\*\*

The metabolic role of the genes is to make enzymes, and each gene is responsible for one, specific enzyme.



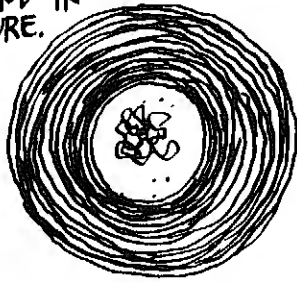
IN SHORT:  
**ONE GENE,  
ONE ENZYME !!**

SO THAT'S WHAT GENES DO—MAKE ENZYMES—BUT STILL NOBODY UNDERSTOOD EXACTLY WHAT THEY **WERE**... THOUGH A FIRST STEP IN THAT DIRECTION HAD BEEN MADE IN THE 1920'S BY **FRED GRIFFITH**...

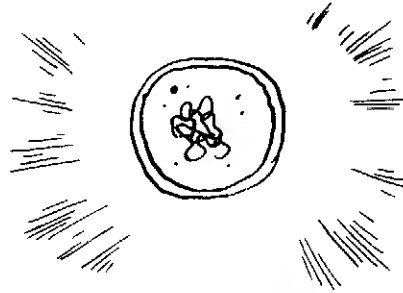
BY ACCIDENT, REALLY!



GRIFFITH WORKED WITH TWO STRAINS OF THE PNEUMONIA BACTERIUM **PNEUMOCOCCUS**. ONE WAS THE VIRULENT "WILD TYPE" FOUND IN NATURE.



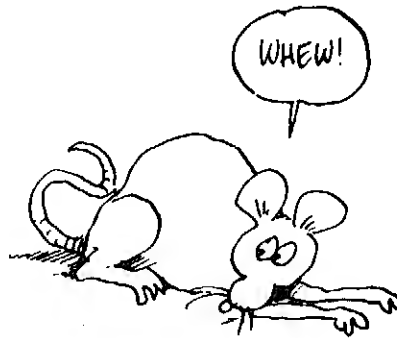
THE OTHER LACKED A CERTAIN ENZYME USED IN MAKING THE THICK OUTER CAPSULE SEEN IN THE WILD TYPE.



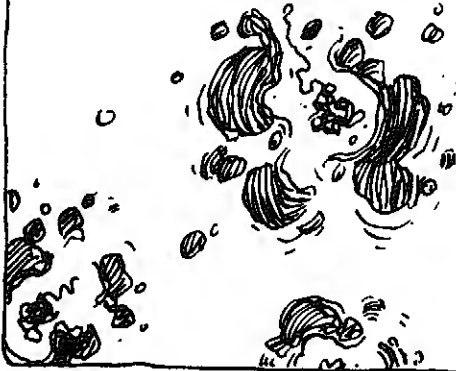
WHEN INJECTED INTO MICE, THE WILD TYPE INVARIABLY CAUSED DISEASE...



THE MUTANT **PNEUMOCOCCUS**, ON THE OTHER HAND, HAD NO EFFECT.



NOW GRIFFITH BOILED SOME OF THE WILD TYPE, MANGLING AND KILLING THEM.



AS EXPECTED, THESE HEAT-KILLED BACTERIA DID NO HARM.

ARE YOU KIDDING?  
MY NERVES  
ARE SHOT!!



THEN, JUST TO BE THOROUGH, GRIFFITH MIXED SOME **HEAT-KILLED WILD TYPE** WITH **LIVE MUTANTS**.



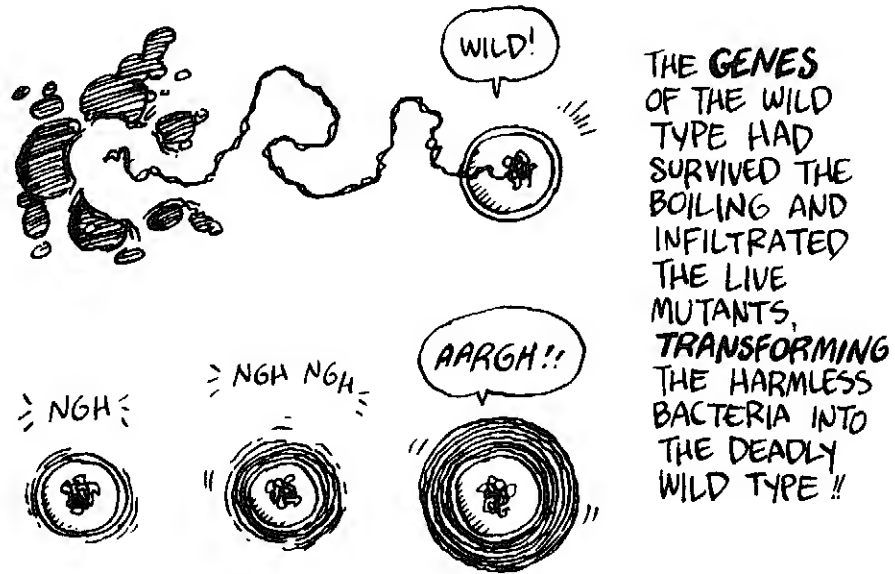
DESPITE THE FACT THAT EACH INGREDIENT WAS HARMLESS IN ITSELF —



NOT ONLY DID THE MICE DIE, BUT **LIVE WILD-TYPE PNEUMOCOCCUS** WERE FOUND IN THEIR BODIES! GRIFFITH COULDN'T FIGURE THIS OUT AT ALL !!!



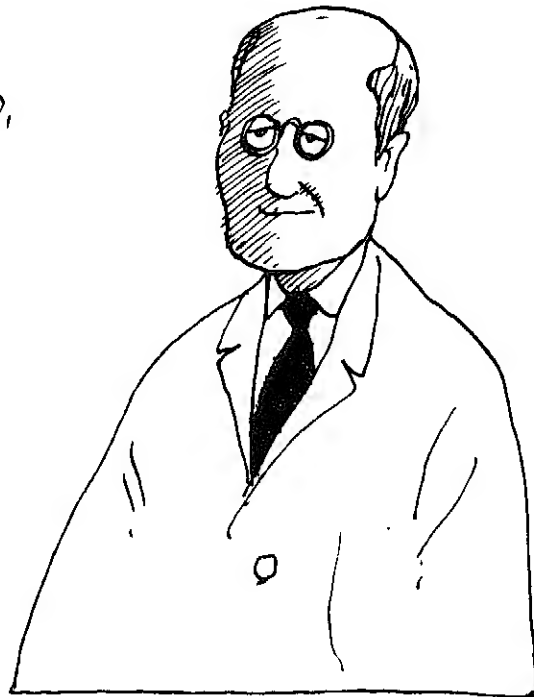
EVENTUALLY, IT WAS UNDERSTOOD THIS WAY:

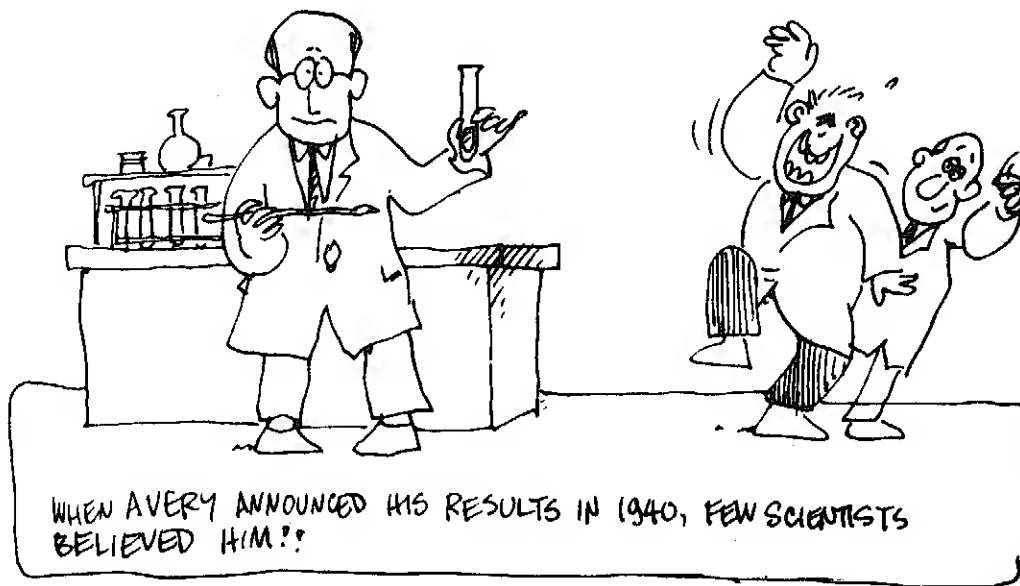


IN THE 1940'S, OSWALD AVERY SET OUT TO IDENTIFY THIS "TRANSFORMING FACTOR:"

BOILING BACTERIA  
BY THE VATFUL,  
AVERY PRECIPITATED,  
EXTRACTED,  
CENTRIFUGED,  
ANALYZED,  
OVER AND OVER...

UNTIL HE HAD  
A THIMBLEFUL  
OF PURE  
GENETIC  
MATERIAL...







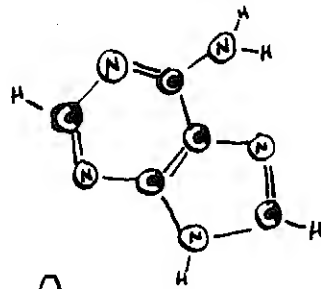
# THE SPIRAL STAIRCASE



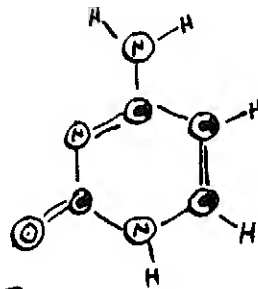
BEFORE AVERY,  
SCIENTISTS HAD  
PAID LITTLE  
ATTENTION TO DNA.

THEY KNEW IT  
CONTAINED THE SUGAR  
**DEOXYRIBOSE**,  
PLENTY OF **PHOSPHATE**,  
AND FOUR **BASES**.

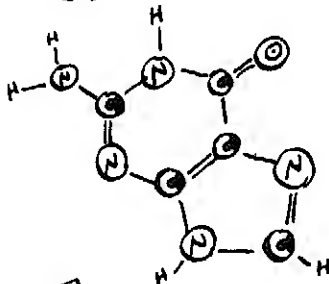
THE FOUR BASES ARE KNOWN AS **A, C, G, AND T**, WHICH  
ARE SHORT FOR:



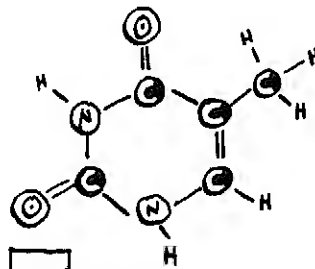
**A**DENINE



**C**YTOSINE



**G**UANINE



**T**HYMINE

THESE WERE ASSUMED TO BE PRESENT IN EQUAL PROPORTIONS.

AFTER AVERY, HOWEVER, RESEARCHERS BEGAN TO LOOK MORE CLOSELY...

### ERWIN CHARGAFF FOUND.



- ① THE COMPOSITION OF DNA VARIED FROM ONE SPECIES TO ANOTHER, IN PARTICULAR IN THE RELATIVE AMOUNTS OF THE BASES A, C, T, G.
- ② IN ANY DNA, THE NUMBER OF A'S WAS THE SAME AS THE NUMBER OF T'S; SIMILARLY, THE NUMBER OF C'S WAS EQUAL TO THE NUMBER OF G'S.

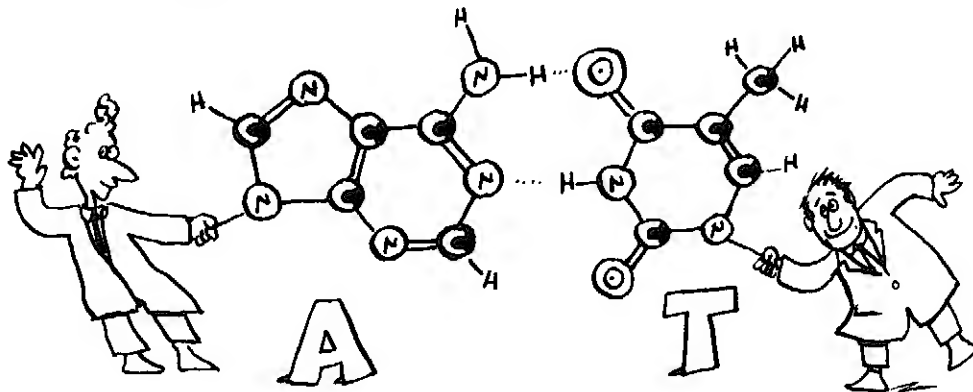
WHAT DID THIS MEAN?  
CHARGAFF COULDN'T SAY..

BY STUDYING X-RAY PICTURES OF DNA, ROSALIND FRANKLIN WAS ABLE TO SHOW THAT THE DNA MOLECULE PROBABLY HAD THE CORKSCREW SHAPE OF A **HELIX** WITH TWO OR THREE CHAINS...

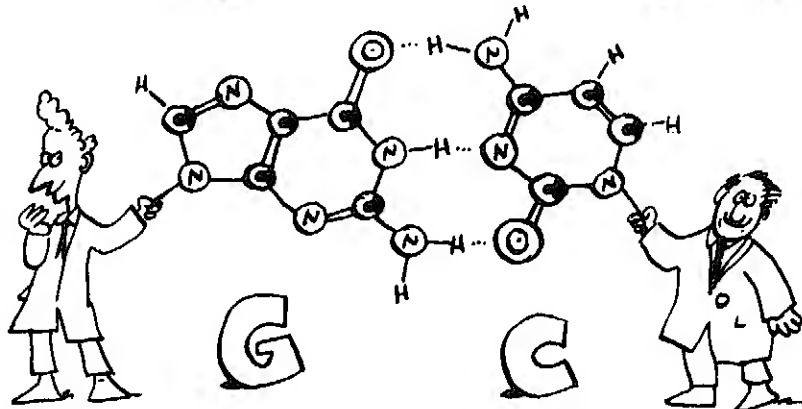
BUT WAS IT TWO OR THREE...?



IN 1952 JAMES WATSON AND FRANCIS CRICK CRACKED THE PUZZLE.



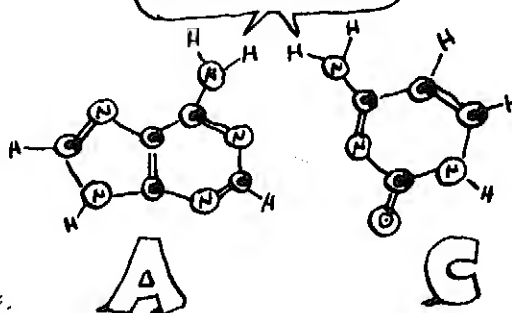
BY PLAYING WITH SCALE-MODEL ATOMS, THEY OBSERVED THAT **ADENINE** FITTED TOGETHER WITH **THYMINE**, WHILE **GUANINE** PAIRED NATURALLY WITH **CYTOSINE**.



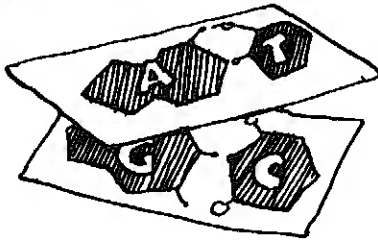
EACH BASE PAIR WOULD BE HELD TOGETHER BY **HYDROGEN BONDING**, A WEAK ATTRACTION THAT MAY OCCUR BETWEEN A HYDROGEN ON ONE MOLECULE AND A NON-HYDROGEN ATOM ON ANOTHER MOLECULE.

IT WAS ALSO CLEAR **A** DID NOT FIT WITH **C**, NOR **G** WITH **T**.

YOU REPEL ME!!



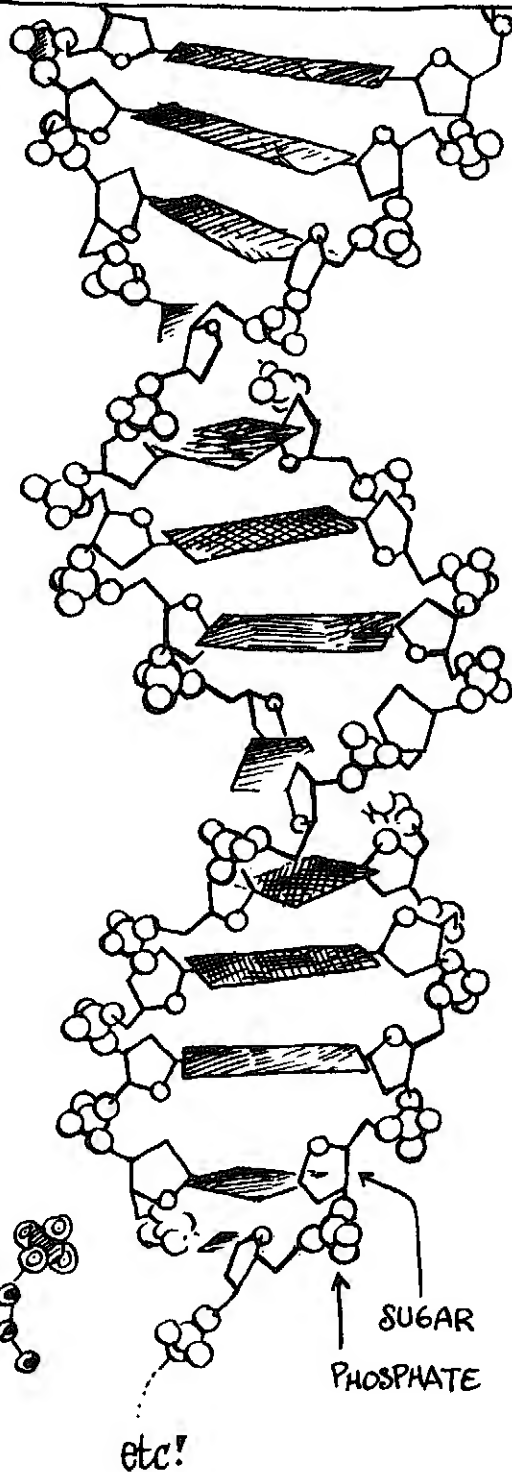
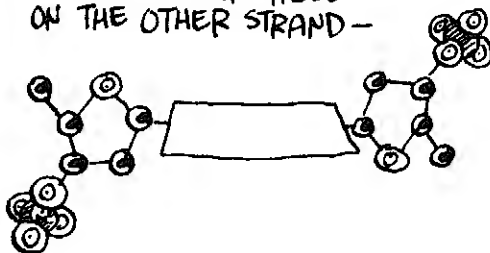
EACH OF THESE TWO  
**BASE PAIRS** IS  
NEARLY FLAT:

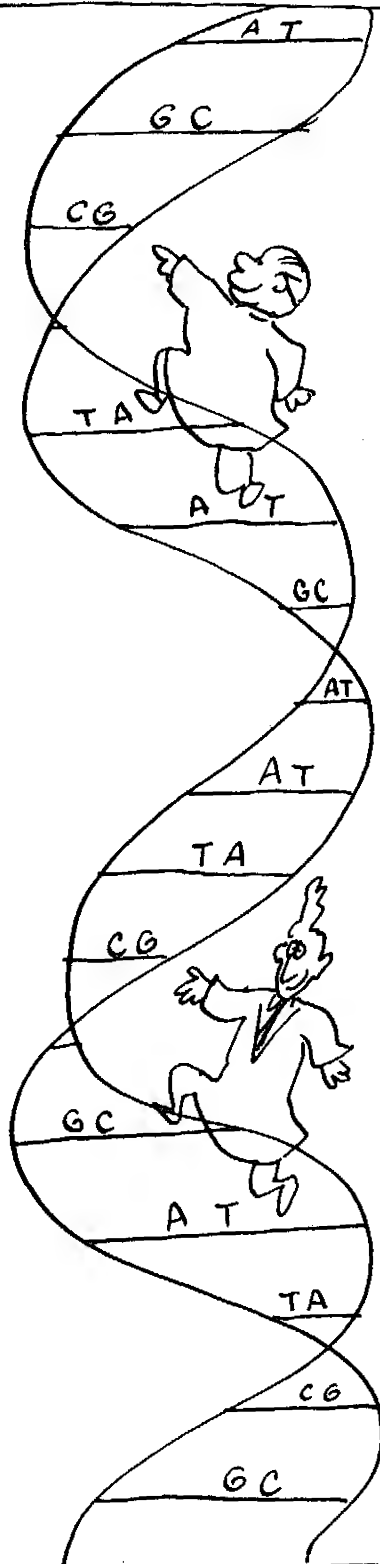


SO WATSON AND  
CRICK PROPOSED TO  
STACK THEM UP,  
ONE AFTER ANOTHER,  
LIKE STAIRSTEPS.  
TWO SUGAR-PHOSPHATE  
STRANDS WIND  
AROUND THE  
OUTSIDE.



ONE COMPLICATION:  
THE TWO STRANDS  
WIND IN **OPPOSITE**  
DIRECTIONS: THE  
SUGARS ON ONE STRAND  
ARE "UPSIDE DOWN"  
COMPARED WITH THOSE  
ON THE OTHER STRAND—





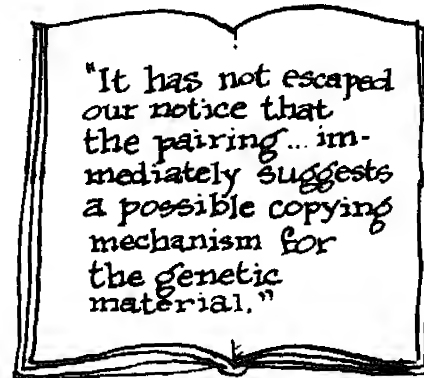
THIS MODEL CLEARLY EXPLAINS CHARGAFF'S OBSERVATION THAT THE NUMBER OF T'S IS EQUAL TO THE NUMBER OF A'S: T AND A ARE ALWAYS PAIRED TOGETHER!

DITTO FOR G AND C!



THIS IS THE PRINCIPLE OF COMPLEMENTARITY: EACH BASE CAN PAIR WITH ONLY ONE OTHER, CALLED ITS COMPLEMENT.

WATSON AND CRICK GOT THE IDEA!! THEY WROTE:

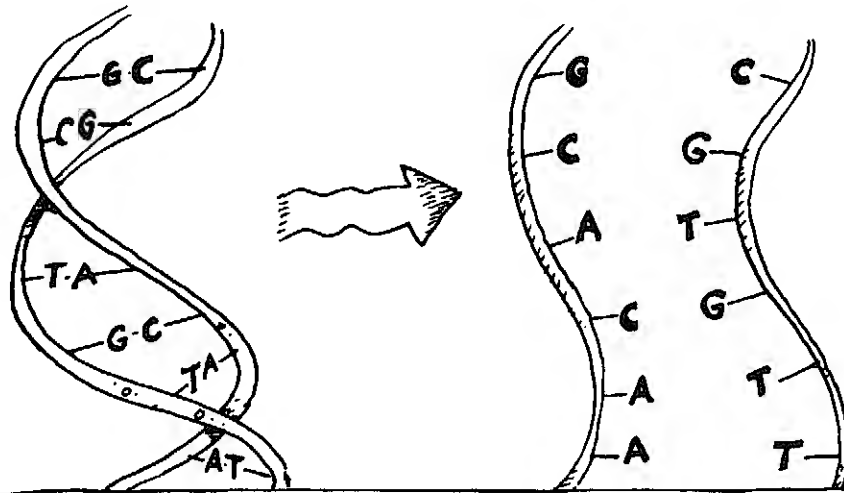


IN FACT, IT IS THE KEY TO THE GENE'S MAIN FUNCTIONS: REPLICATION AND PROTEIN SYNTHESIS.

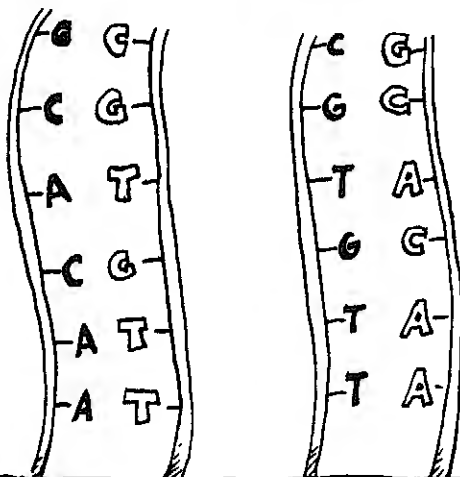
# REPLICATION

GENE COPYING, OR DNA REPLICATION, AS WATSON AND CRICK SAW, IS SIMPLE IN PRINCIPLE. EACH STRAND OF THE DOUBLE HELIX CONTAINS THE INFORMATION NECESSARY TO MAKE ITS COMPLEMENTARY STRAND.

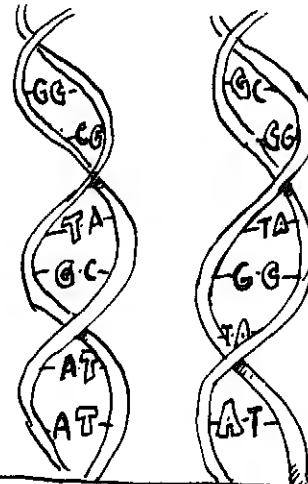
SCHEMATICALLY, IT WORKS LIKE THIS: WHEN THE DNA IS READY TO MULTIPLY, ITS TWO STRANDS PULL APART:

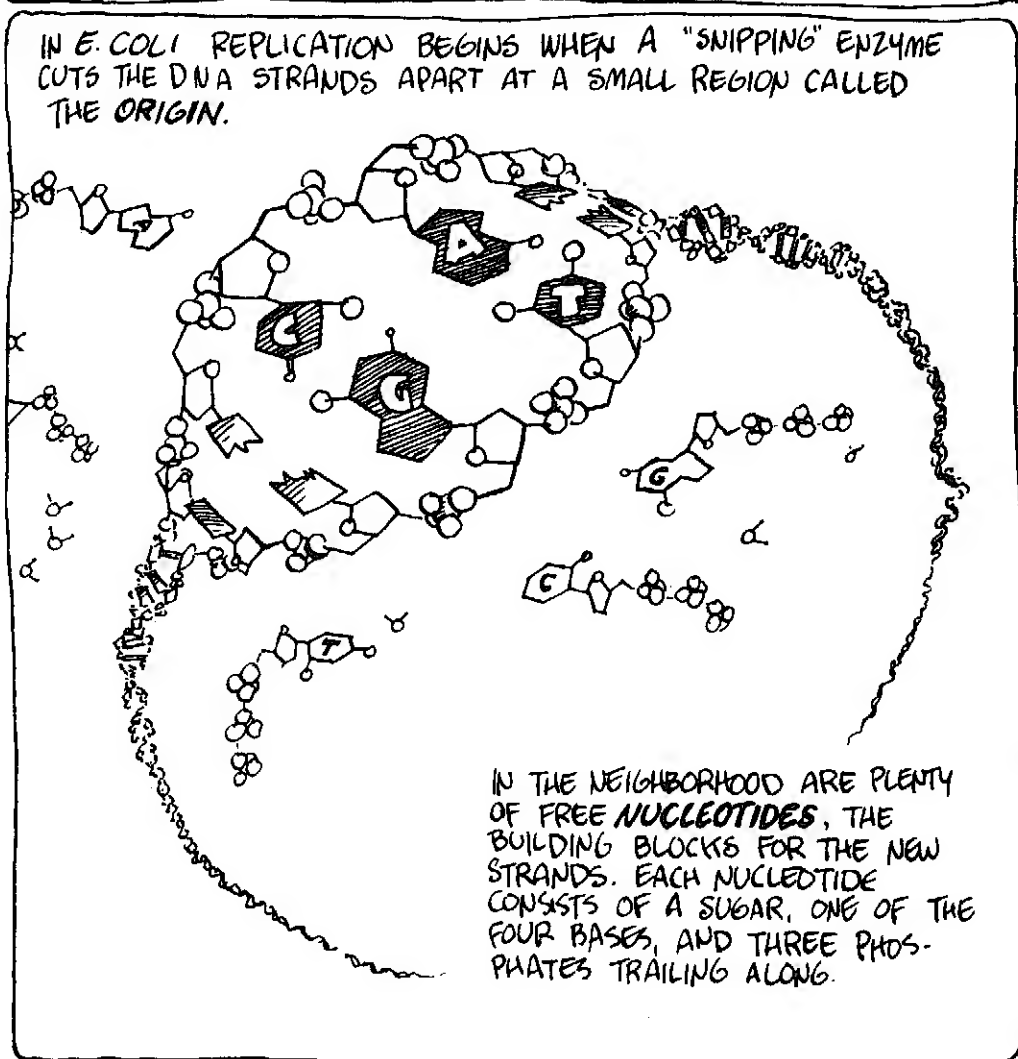
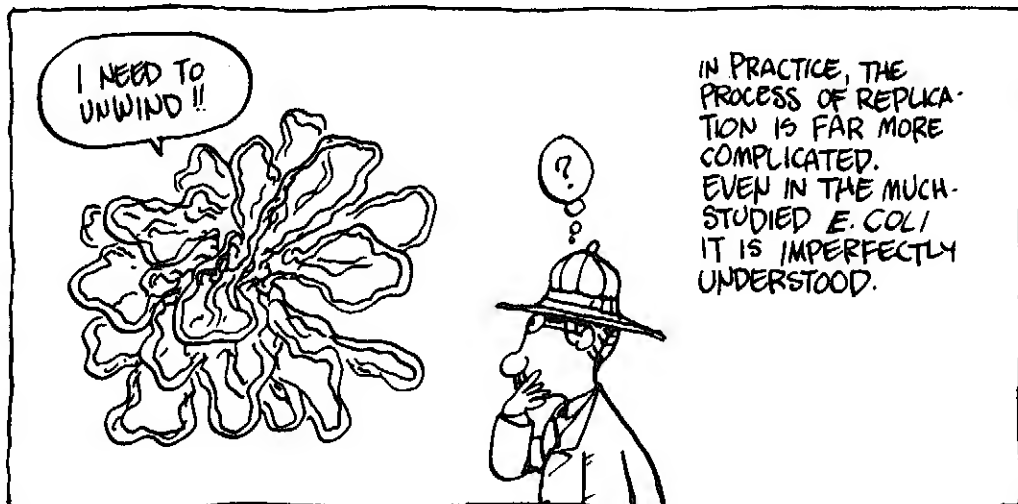


ALONG EACH ONE, A NEW STRAND FORMS IN THE ONLY POSSIBLE WAY:

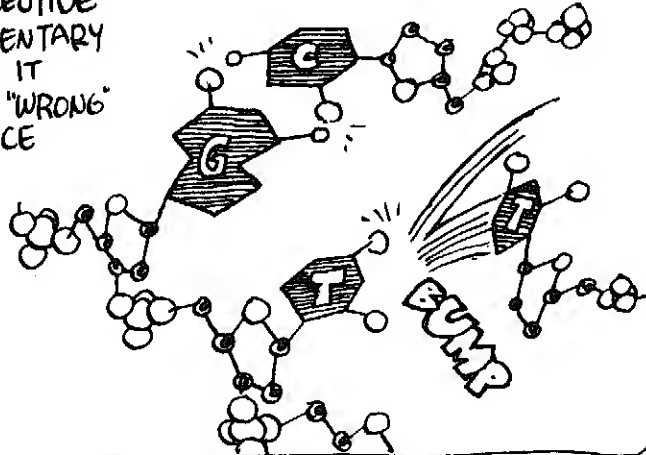


WE WIND UP WITH TWO COPIES OF THE ORIGINAL!

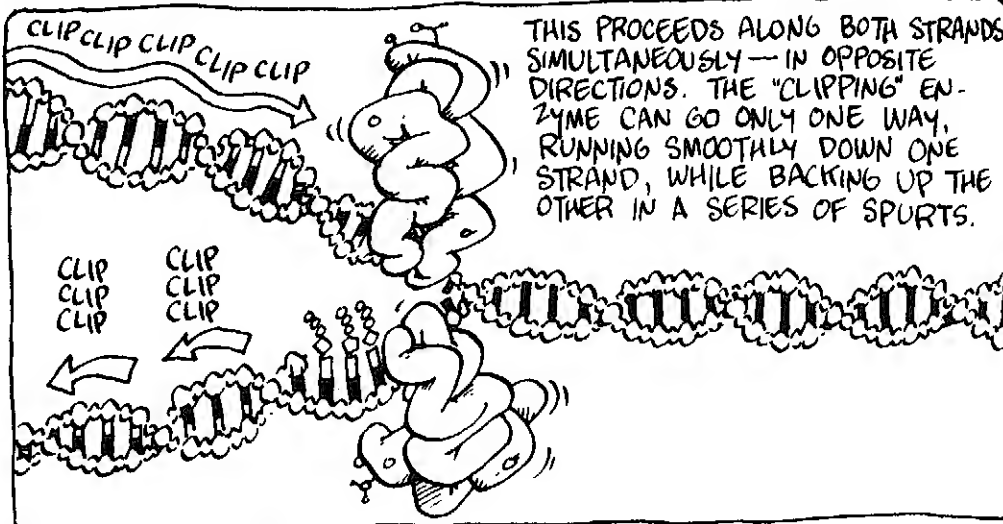
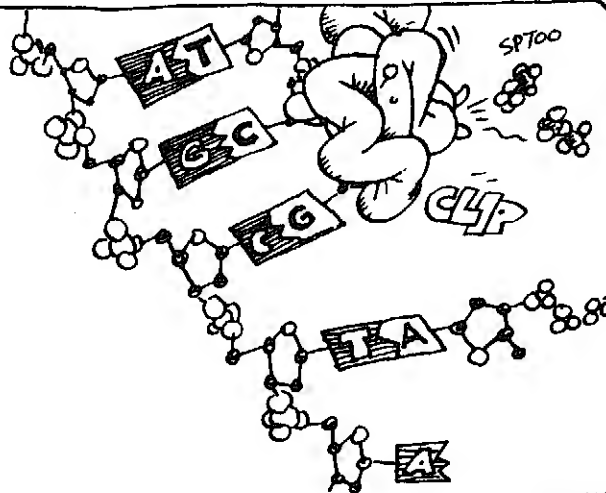




WHEN A FREE NUCLEOTIDE MEETS ITS COMPLEMENTARY BASE ON THE DNA, IT STICKS, WHILE THE "WRONG" NUCLEOTIDES BOUNCE AWAY.



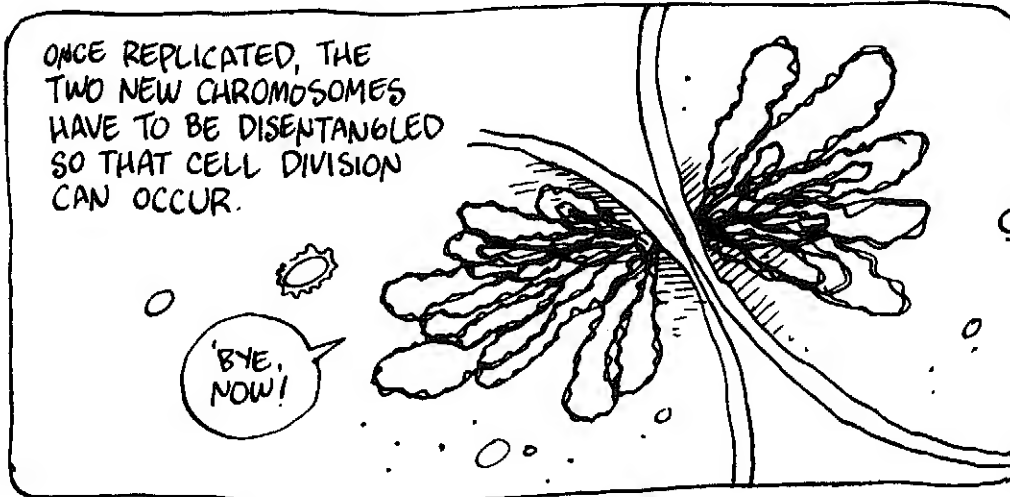
AS THE "SNIPPING" ENZYME OPENS THE DNA FURTHER, MORE NUCLEOTIDES ARE ADDED, AND A "CLIPPING" ENZYME PUTS THEM TOGETHER, KNOCKING OFF THE EXTRA PHOSPHATES.



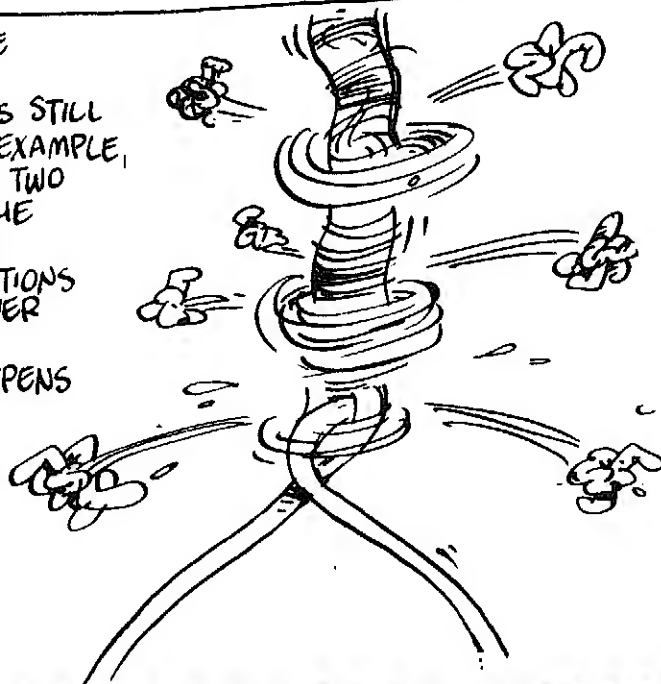
THIS PROCEEDS ALONG BOTH STRANDS SIMULTANEOUSLY — IN OPPOSITE DIRECTIONS. THE "CLIPPING" ENZYME CAN GO ONLY ONE WAY, RUNNING SMOOTHLY DOWN ONE STRAND, WHILE BACKING UP THE OTHER IN A SERIES OF SPURTS.



ONCE REPLICATED, THE TWO NEW CHROMOSOMES HAVE TO BE DISENTANGLED SO THAT CELL DIVISION CAN OCCUR.



THE PICTURE WE HAVE OF DNA REPLICATION IS STILL SKETCHY. FOR EXAMPLE, UNWINDING THE TWO STRANDS OF THE DOUBLE HELIX INVOLVES ROTATIONS AT SPEEDS OVER 8000 RPM. HOW THIS HAPPENS IS STILL NOT WELL UNDERSTOOD.



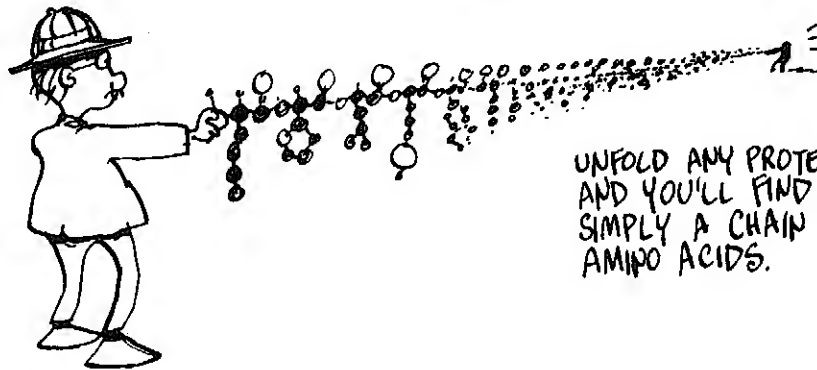
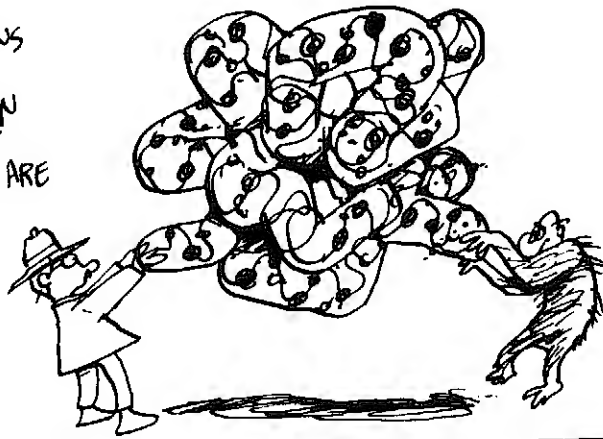
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WHATEVER THE DETAILS, THE PRINCIPLE OF COMPLEMENTARITY IS THE KEY TO REPLICATION, AS WELL AS TO THE GENE'S SECOND MAIN FUNCTION:



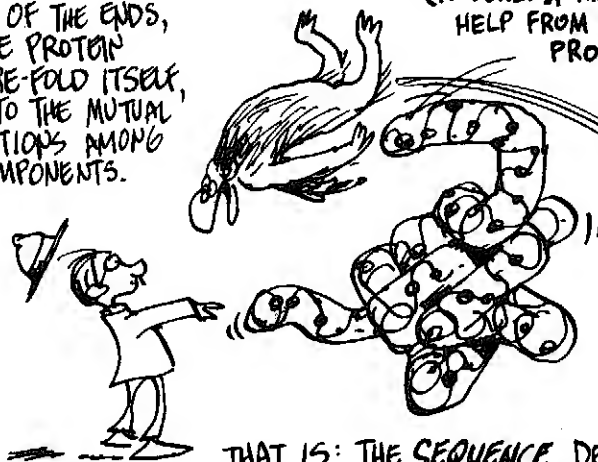
# The MOLECULE is the MESSAGE

ENZYMES AND OTHER PROTEINS COME IN MANY SHAPES, BUT IN AN IMPORTANT RESPECT, THEY ARE ALL ALIKE.



UNFOLD ANY PROTEIN, AND YOU'LL FIND IT'S SIMPLY A CHAIN OF AMINO ACIDS.

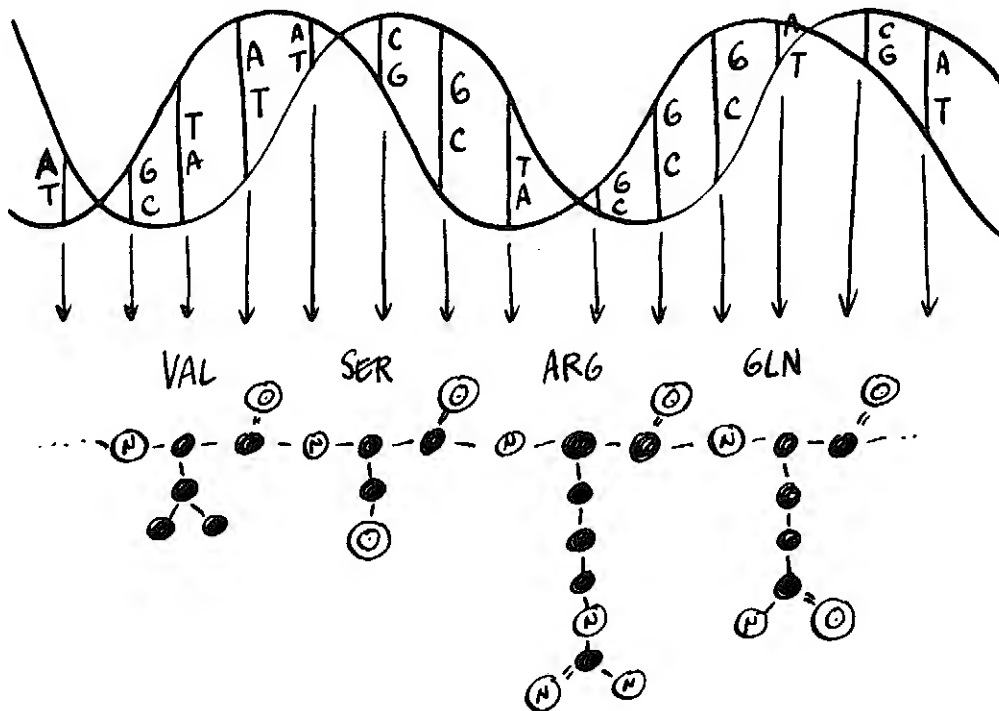
LET GO OF THE ENDS, AND THE PROTEIN WILL RE-FOLD ITSELF, OWING TO THE MUTUAL ATTRACTIONS AMONG THE COMPONENTS.



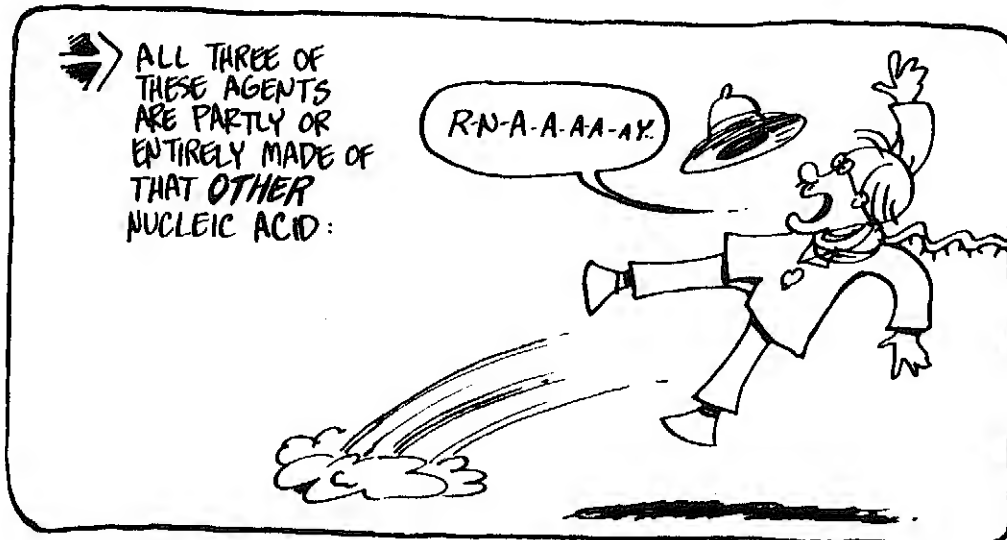
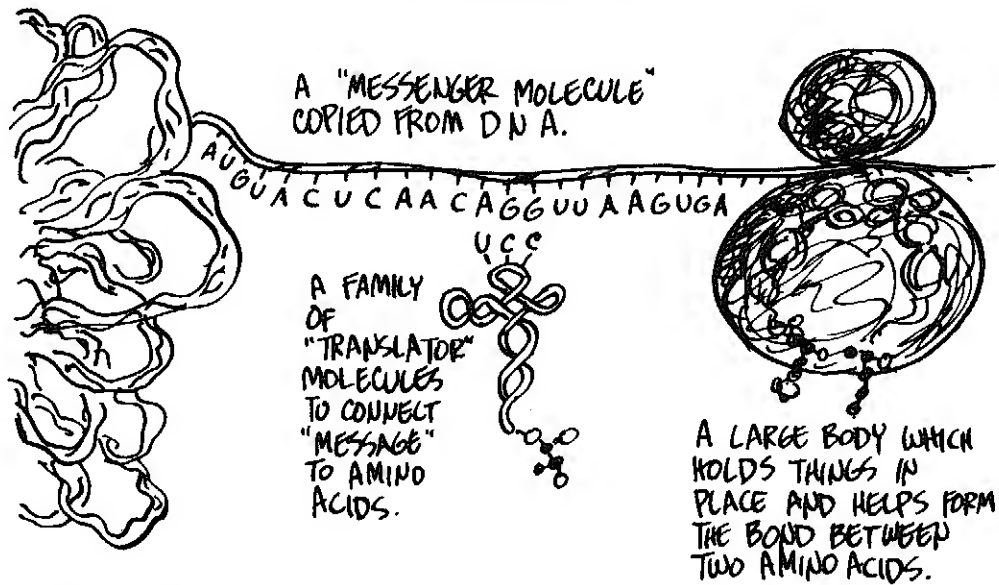
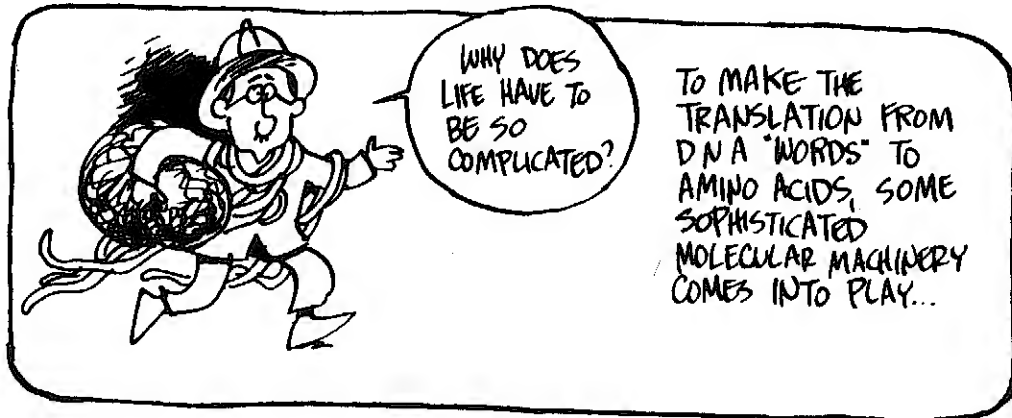
(ACTUALLY, MANY PROTEINS NEED HELP FROM ANOTHER "CHAPERONE" PROTEIN TO FOLD UP.)

THAT IS: THE SEQUENCE DETERMINES THE STRUCTURE.

IN VIEW OF THE RELATIONSHIP BETWEEN GENES AND PROTEINS, THIS SUGGESTS THAT THE *SEQUENCE* OF DNA MUST SOMEHOW PARALLEL OR REFLECT THE *SEQUENCE* OF THE PROTEIN.



The sequence of base pairs may be thought of as a series of "words" specifying the order of amino acids in each protein.



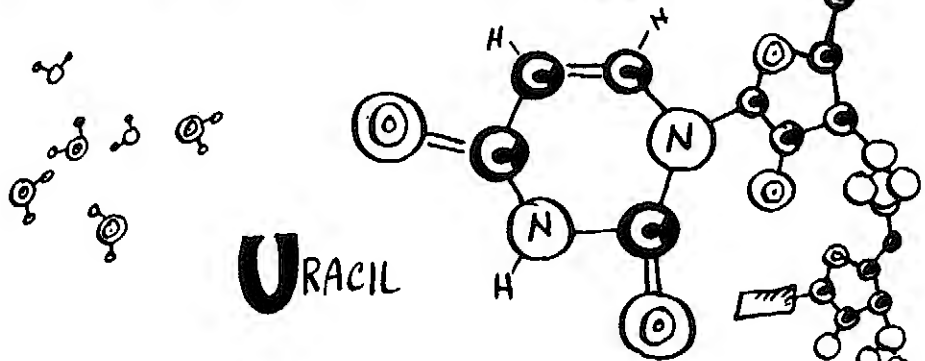
RNA — **RIBONUCLEIC ACID** — RESEMBLES  
DNA: A SUGAR-PHOSPHATE BACKBONE  
WITH A SERIES OF BASES ATTACHED.



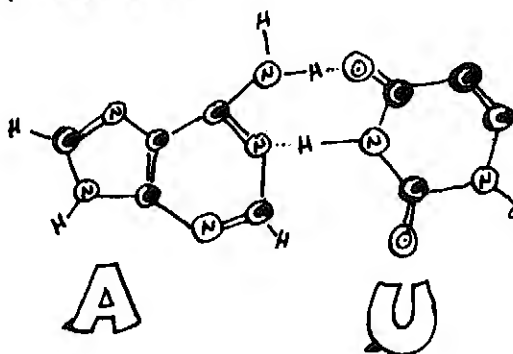
THE  
DIFFERENCES:

ITS SUGAR IS **RIBOSE**,  
RATHER THAN DEOXYRIBOSE;  
RNA IS USUALLY  
**SINGLE-STRANDED**;  
AND IT IS MUCH SHORTER —  
50 TO 1000 NUCLEOTIDES,  
COMPARED WITH A  
MILLION OR MORE IN DNA!

AND FINALLY, WHILE THE BASES **A, C, AND G**  
ARE THE SAME AS IN DNA, RNA HAS IN  
PLACE OF **T** ANOTHER BASE CALLED **URACIL** ("U").



WHICH, LIKE **THYMINE**, IS COMPLEMENTARY  
TO **ADENINE**:

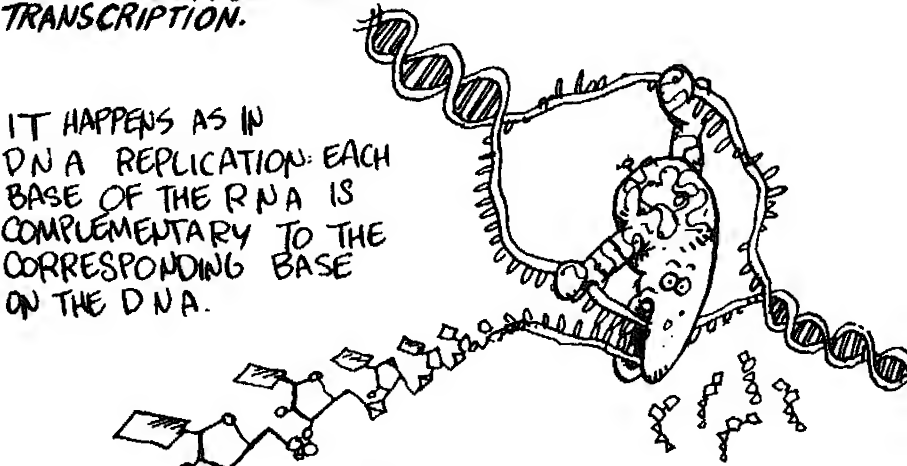


NOW LET'S  
SEE HOW  
RNA  
WORKS !!



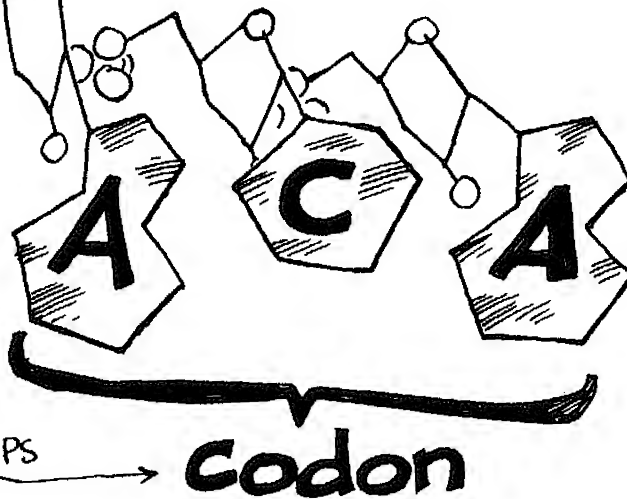
PROTEIN SYNTHESIS BEGINS WHEN A REGION OF DNA IS TEASED APART AND A MOLECULE OF RNA IS BUILT ALONG ONE STRAND BY AN ENZYME CALLED **RNA POLYMERASE**. THIS PROCESS IS CALLED **TRANSCRIPTION**.

IT HAPPENS AS IN DNA REPLICATION: EACH BASE OF THE RNA IS COMPLEMENTARY TO THE CORRESPONDING BASE ON THE DNA.



THIS RNA IS CALLED THE **MESSENGER**, OR **mRNA**, BECAUSE IT CARRIES THE GENETIC MESSAGE FROM THE DNA TO THE PROTEIN FACTORY.

THE "WORDS" OF THE MESSAGE ARE **TRIPLETS OF BASES** — A-U-G, A-C-A, ETC. THE TECHNICAL NAME FOR ONE OF THESE GROUPS IS A



EACH 3-BASE CODON STANDS FOR A SINGLE AMINO ACID, AND THE WHOLE mRNA STRAND ENCODES A PROTEIN (OR SEVERAL PROTEINS). IT'S JUST LIKE A MESSAGE IN CODE —




# THE GENETIC CODE!



CRACKING THIS CODE BEGAN IN 1961, WHEN MARSHALL NIRENBERG WAS ABLE TO MAKE A SPECIAL mRNA, WHOSE ONLY BASE WAS URACIL, REPEATED OVER AND OVER. "POLY-U."



FROM IT HE OBTAINED A PROTEIN CONSISTING ENTIRELY OF THE AMINO ACID PHENYLALANINE.

SO  UUU WAS THE CODON FOR PHENYLALANINE...

NEXT THEY DECODED POLY-A, AND POLY-C, AND POLY-UG, POLY-UGU, ETC, ETC, ETC, UNTIL THE CODE WAS FINALLY BROKEN —

UUU	→	Phe
AAA	→	Lys
CCC	→	
UGU	→	
GUU	→	
UUG	→	Leu
GUG	→	Val

THE COMPLETE CODE TABLE FOLLOWS!



		SECOND LETTER					
		U	C	A	G		
FIRST LETTER	U	UUU } PHE UUC } UUA } LEU UUG }	UCU } UCC } SER UCA } UCG }	UAU } TYR UAC } UAA } STOP UAG }	UGU } CYS UGC } UGA } STOP UGG } TRP	U C A G	THIRD LETTER
	C	CUU } CUC } LEU CUA } CUG }	CCU } CCC } PRO CCA } CCG }	CAU } HIS CAC } CAA } GLN CAG }	CGU } CGC } ARG CGA } CGG }	U C A G	
	A	AUU } ILE AUC } AUA } AUG } MET	ACU } ACC } THR ACA } ACG }	AAU } ASN AAC } AAA } LYS AAG }	AGU } SER AGC } AGA } ARG AGG }	U C A G	
	G	GUU } GUC } VAL GUA } GUG }	GCU } GCC } ALA GCA } GCG }	GAU } ASP GAC } GAA } GLU GAG }	GGU } GGC } GLY GGA } GGG }	U C A G	



THE CODE IS REDUNDANT: WITH 64 POSSIBLE CODONS, BUT ONLY 20 AMINO ACIDS, THERE MUST BE "SYNONYMS," DIFFERENT CODONS WHICH ENCODE THE SAME AMINO ACID.

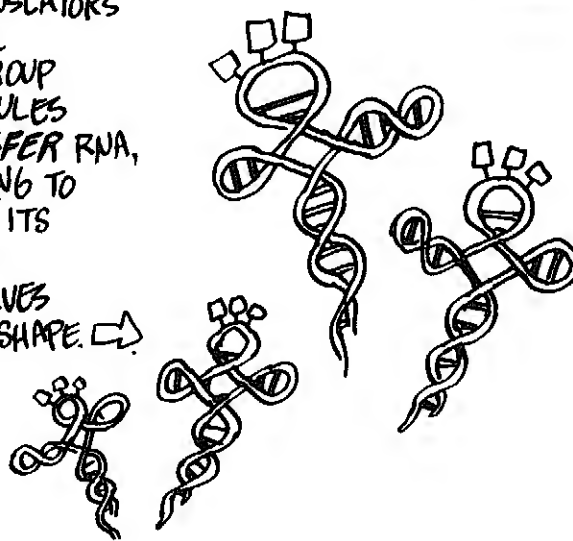
THERE ARE "STOP" SIGNALS. THREE CODONS DO NOT ENCODE ANY AMINO ACID AT ALL. THESE SERVE TO TERMINATE MESSAGES.

**ALSO:** THE CODE IS NON-OVERLAPPING. THE "WORDS" FOLLOW EACH OTHER WITHOUT GAPS OR OVERLAPS. WE'LL SEE SHORTLY HOW IT KNOWS WHERE TO START...

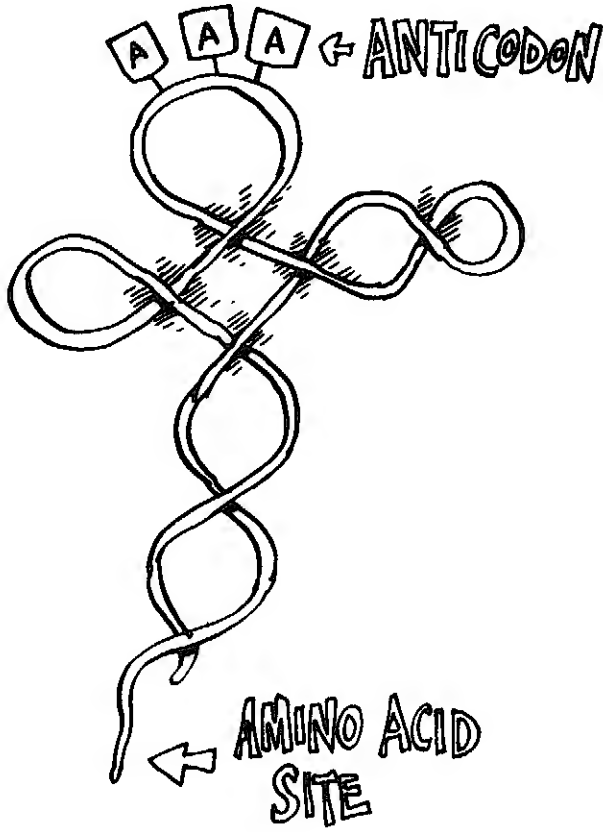




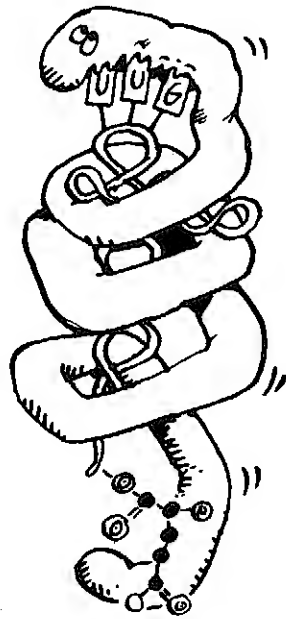
THE ACTUAL TRANSLATORS OF THE GENETIC CODE ARE A GROUP OF RNA MOLECULES CALLED TRANSFER RNA, OR tRNA. DUE TO PAIRING AMONG ITS BASES, tRNA'S TWIST THEMSELVES INTO THIS KEY SHAPE. →



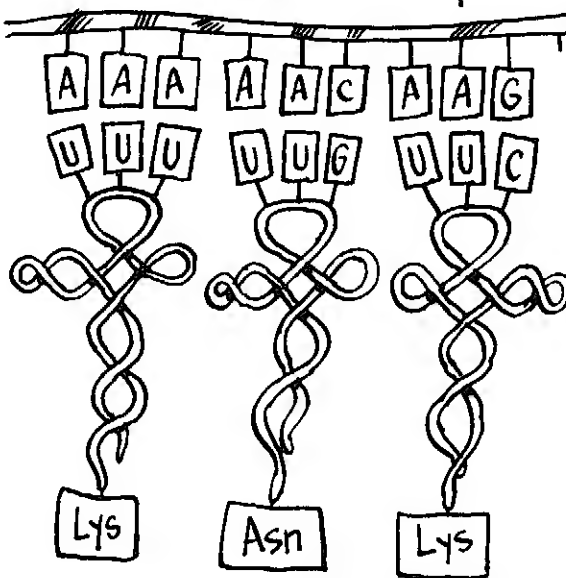
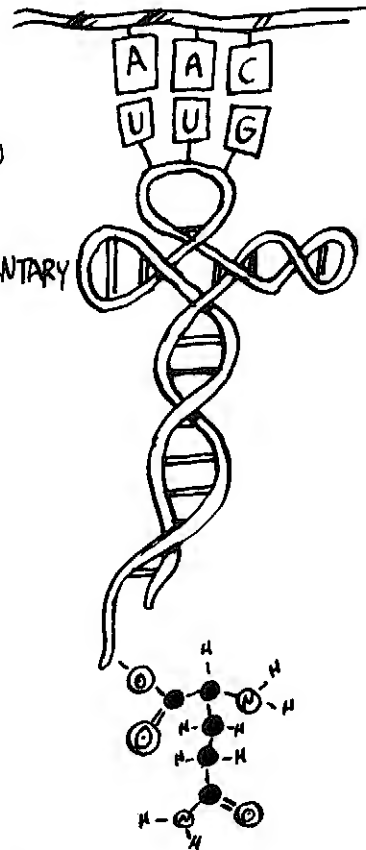
THE LOOP END OF tRNA HAS THREE UNPAIRED BASES. THIS "ANTICODON" MAY BIND WITH THE COMPLEMENTARY CODON OF mRNA. AT THE "TAIL" END OF tRNA IS A SITE FOR ATTACHING A SINGLE AMINO ACID.



FOR EACH ANTICODON, THERE IS AN ENZYME WHICH RECOGNIZES IT AND ATTACHES THE APPROPRIATE AMINO ACID TO ITS tRNA.



ONCE THEY ARE LINKED, THE ANTICODON BINDS TO THE COMPLEMENTARY CODON OF MESSAGE.



SCHEMATICALLY, THIS IS THE WAY A STRING OF BASES IS TRANSLATED INTO A SEQUENCE OF AMINO ACIDS.

**HOWEVER,** THE CELL NEEDS ONE MORE PIECE OF EQUIPMENT TO MAKE IT WORK: THE RIBOSOME.

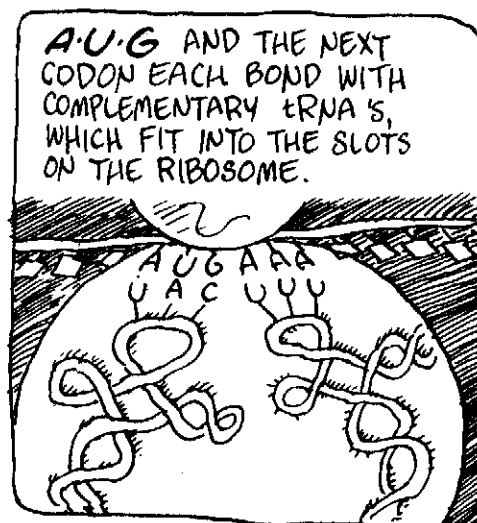
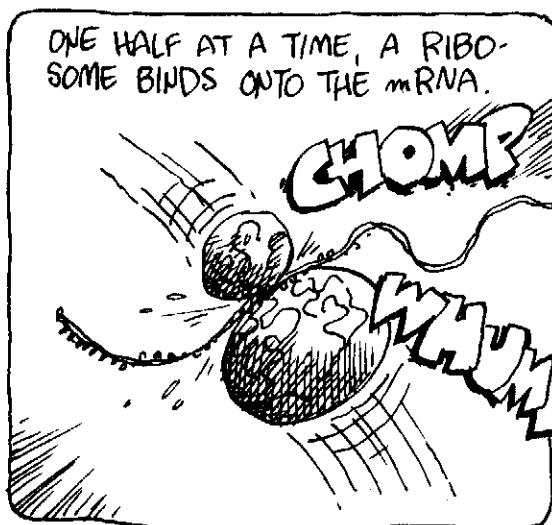
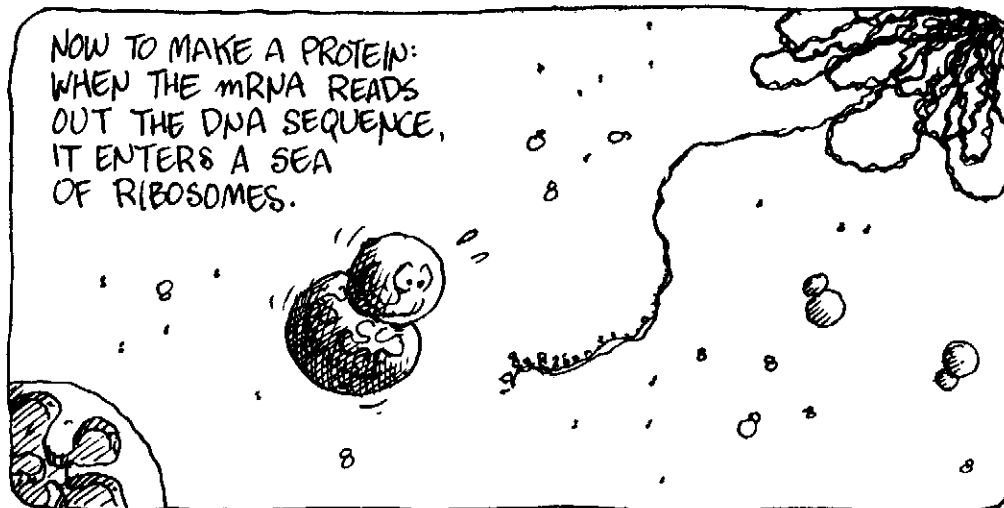
# HOW PROTEINS ARE MADE

THE FINAL INGREDIENT IN THE PROTEIN-MAKING APPARATUS IS AN OBJECT THAT HOLDS EVERYTHING IN PLACE.

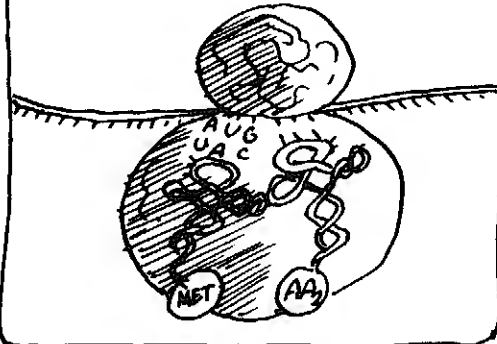
THIS IS THE **RIBOSOME**, A DOUBLE BALL OF ABOUT 50 PROTEINS WRAPPED UP WITH RNA. THIS RNA IS CALLED **RIBOSOMAL RNA**, rRNA FOR SHORT.



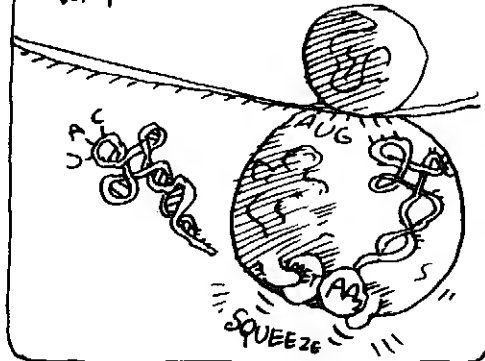
THE RIBOSOME HAS TWO SLOTS IN WHICH MOLECULES OF tRNA CAN FIT SNUGLY.



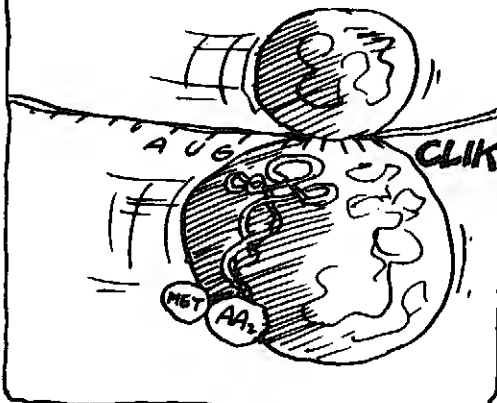
EACH tRNA CARRIES AN AMINO ACID (AA), THE FIRST ONE ALWAYS BEING METHIONINE, WHICH GOES WITH A·U·G.



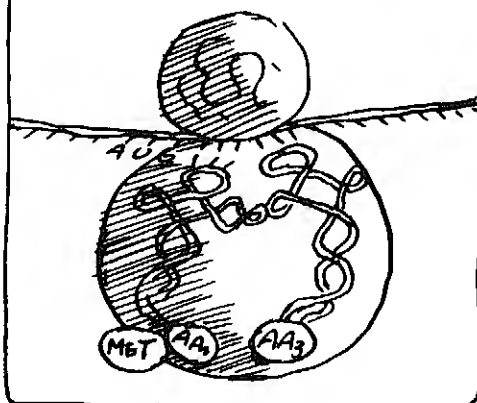
AN ENZYME IN THE RIBOSOME LINKS THE TWO AMINO ACIDS, AND THE FIRST tRNA FLOATS AWAY.



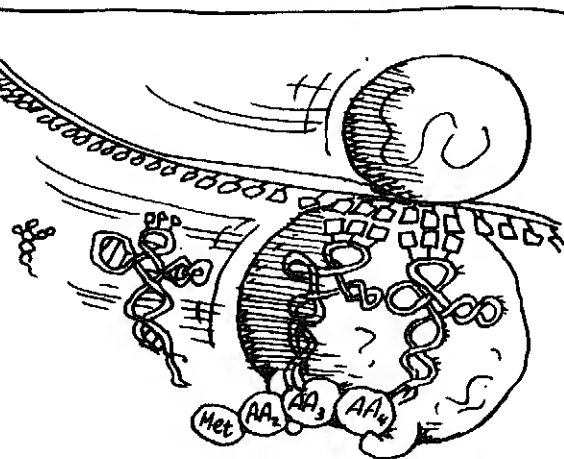
THE RIBOSOME THEN MOVES DOWN THREE MORE BASES.



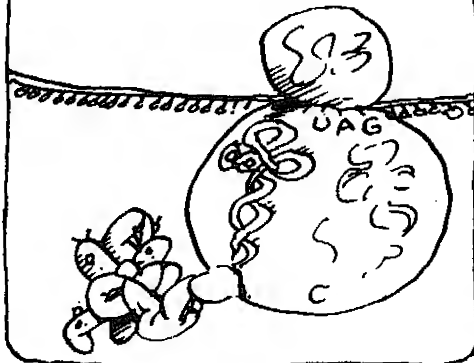
ANOTHER tRNA AND AMINO ACID BIND ON.



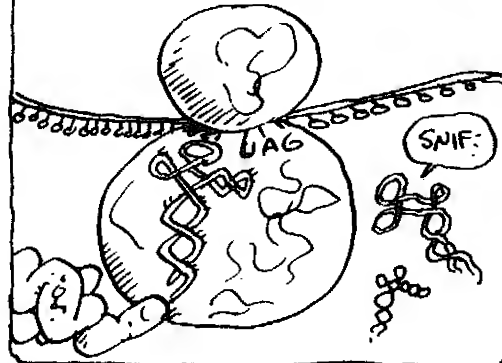
THE AMINO ACIDS ARE LINKED; THE "EMPTY" tRNA IS DISCARDED; AND SO THE RIBOSOME MOVES ALONG THE MESSAGE, PILING UP AMINO ACIDS, WHICH FOLD THEMSELVES INTO A PROTEIN.



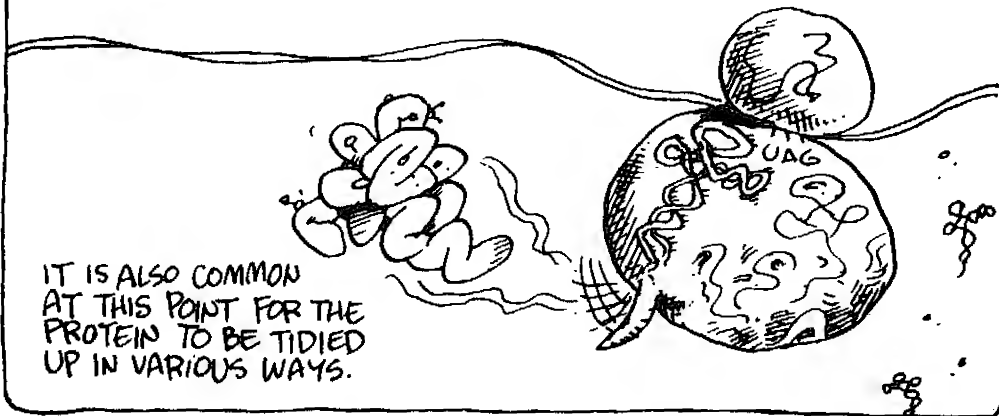
THIS PROCESS CONTINUES UNTIL THE RIBOSOME REACHES ONE OF THE "STOP" SIGNALS.



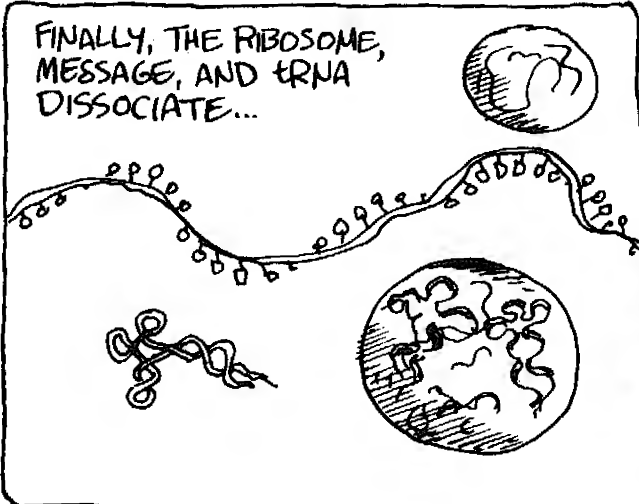
IT STOPS BECAUSE THERE IS NO tRNA WITH AN ANTICODON TO MATCH.



THE COMPLETED PROTEIN IS CLIPPED OFF BY ANOTHER RIBOSOMAL ENZYME.



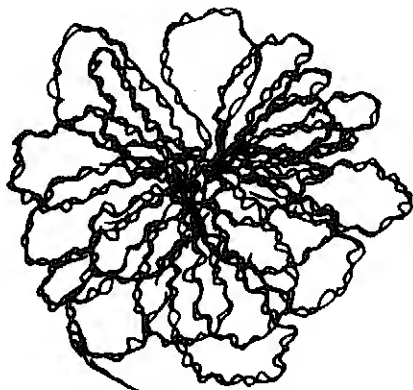
FINALLY, THE RIBOSOME, MESSAGE, AND tRNA DISSOCIATE...



...AND THE NEW MACROMOLECULE GOES OFF TO DO ITS JOB: STRUCTURE, ENZYME, OR WHATEVER...

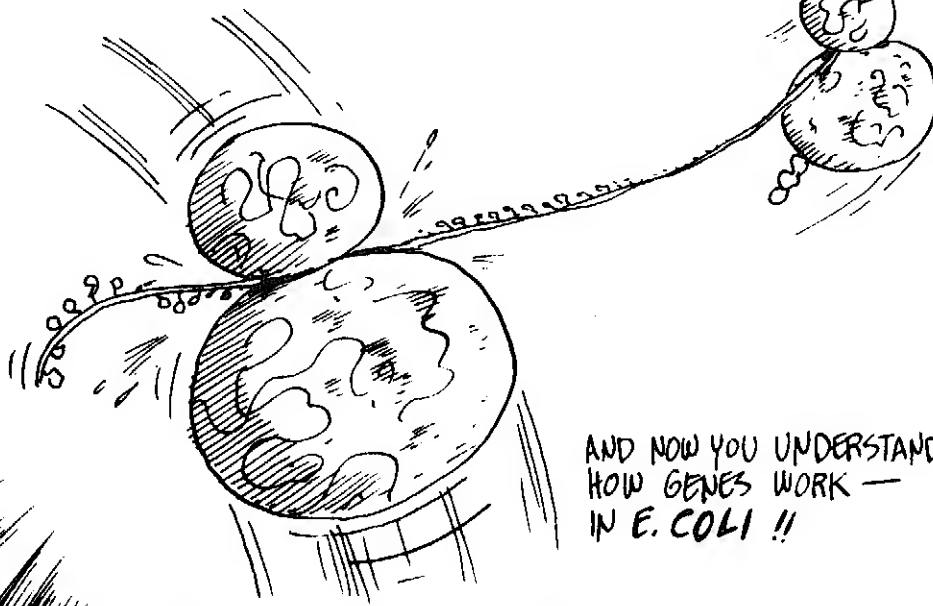


IN THE LIVING CELL, ALL THESE PROCESSES ARE GOING ON TOGETHER. THIS IS HOW IT LOOKS IN *E. COLI*.



IN BACTERIA GENERALLY, PROTEIN-BUILDING BEGINS WHILE THE mRNA IS STILL BEING TRANSCRIBED FROM THE GENE.

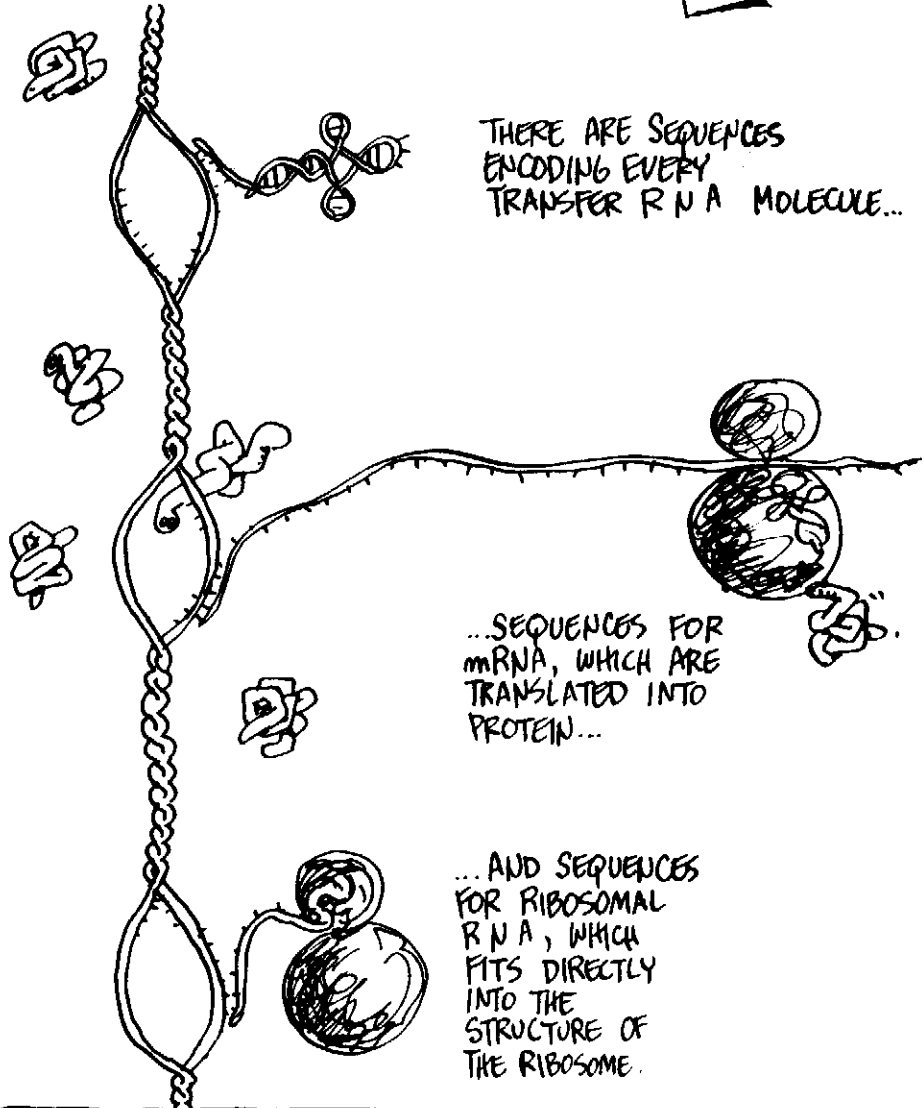
THE MESSAGE IS READ BY SEVERAL RIBOSOMES AT ONCE. NOTE HOW THE PROTEIN FOLDS INTO ITS FINAL FORM AS IT IS BEING ASSEMBLED.



AND NOW YOU UNDERSTAND HOW GENES WORK — IN *E. COLI* !!

**NOTE**

FOR A MOMENT  
HOW MUCH WE'VE  
ALREADY FOUND  
ENCODED IN THE  
CHROMOSOME.



TRULY, THE DNA IS  
THE BLUEPRINT OF  
ALL THE CELL'S  
ESSENTIAL PARTS.

BLUEPRINT?  
WHO'S THE  
ARCHITECT?



ASK  
MENDEL  
...



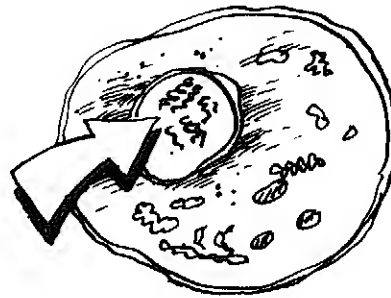
# PRO AND EU

WE BEGAN BY ASKING ABOUT GORILLAS AND BANANAS, AND ENDED UP INSIDE SOME INSIGNIFICANT LITTLE BUG, E. COLI... NOW WHAT CAN WE SAY ABOUT OTHER LIFE FORMS?



FIRST, SOME MORE JARGON: THE CELLS OF PLANTS, ANIMALS, AND OTHER ADVANCED CREATURES — IN FACT, ANY CELL WITH A NUCLEUS — IS CALLED A EUCARYOTE ("YOU-CARRY-OAT"), MEANING "GOOD NUCLEUS" IN GREEK.

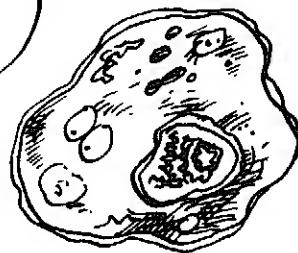
EUCARYOTES CONTAIN ALL SORTS OF BODIES, BUT THE KEY IS THE NUCLEUS, WHICH CONTAINS THE CHROMOSOMES.



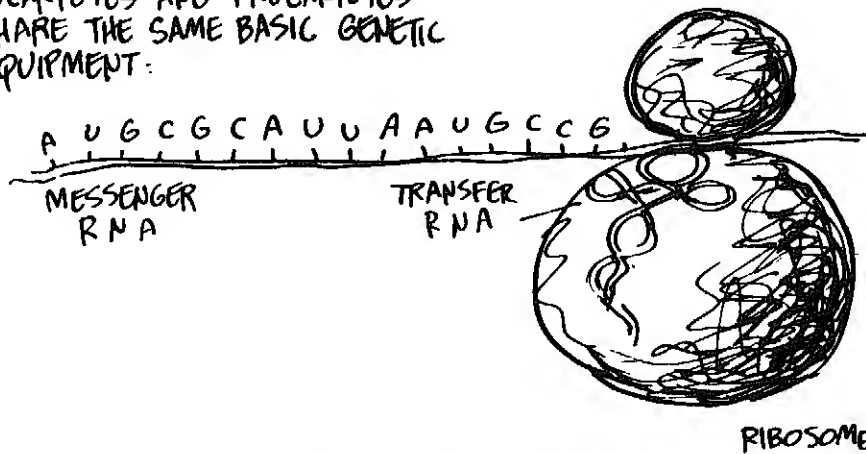
THE TINY BACTERIA, WITH THEIR SIMPLER STRUCTURE, ARE CALLED PROCARYOTES ("PRO-CARRY-OATS"), MEANING "BEFORE NUCLEUS" IN GREEK.

THE IDEA IS THAT PROCARYOTES MUST HAVE EVOLVED BEFORE THE MORE COMPLICATED EUCARYOTES.

SONNY,  
IS THAT  
EU?



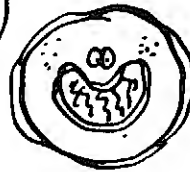
EUCARYOTES AND PROCARYOTES  
SHARE THE SAME BASIC GENETIC  
EQUIPMENT:



**IN ALL LIFE, THE GENETIC  
CODE IS THE SAME —**

A FACT WHICH  
STRONGLY SUGGESTS  
THAT WE ALL  
COME FROM A  
COMMON ANCESTOR.

LET'S HAVE  
A FAMILY  
REUNION  
SOMETIME!



ANYTIME...  
I'LL BRING  
MY GORILLA...



**BUT**

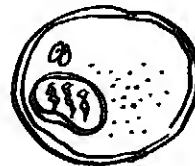
AND EU...

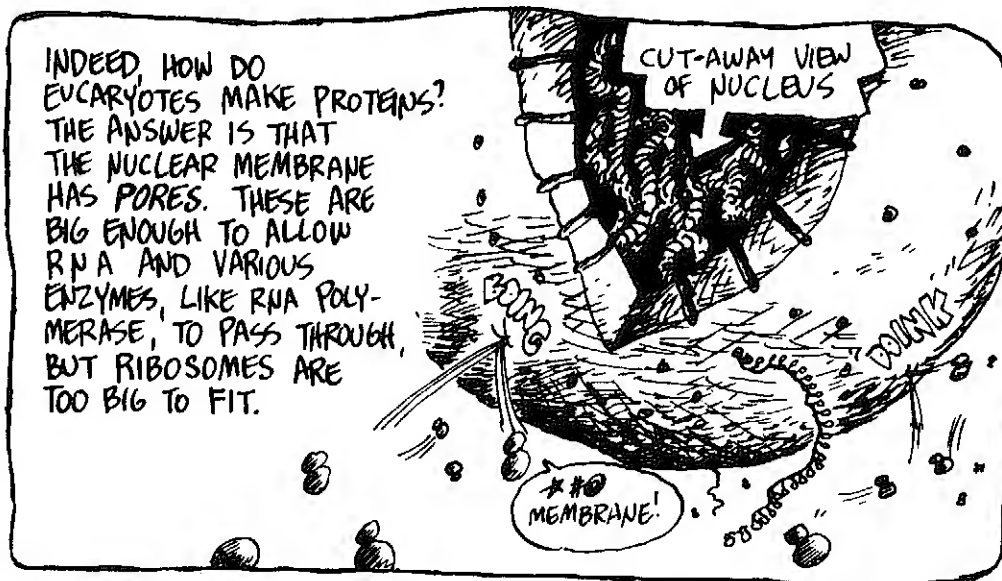
TO BEGIN  
WITH, EUCARYOTES  
HAVE ALL THEIR  
RIBOSOMES  
OUTSIDE THE  
NUCLEUS, SEPARATED  
FROM THE GENES  
BY A MEMBRANE.

HOW CAN  
YOU MAKE  
PROTEINS?

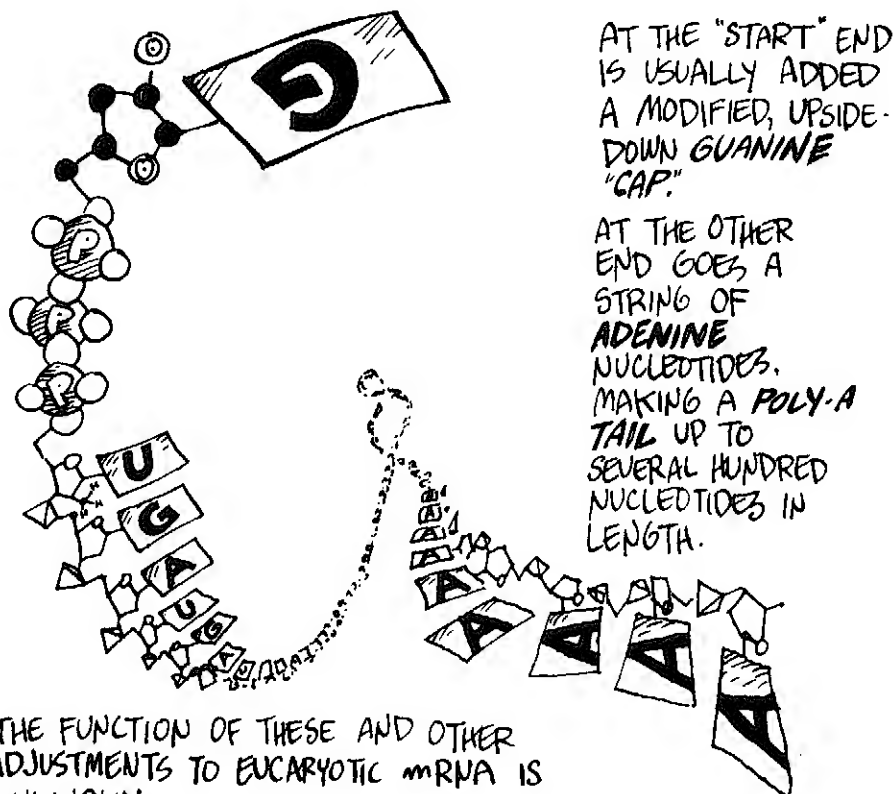


IT'S A BIT  
LIKE KISSING  
THROUGH PLASTIC...



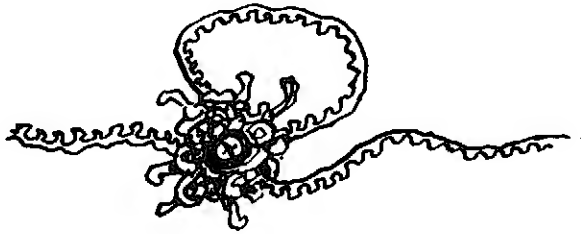


WITHIN THE NUCLEUS, mRNA IS MADE AS IN BACTERIA — BUT THEN COME CERTAIN MODIFICATIONS...

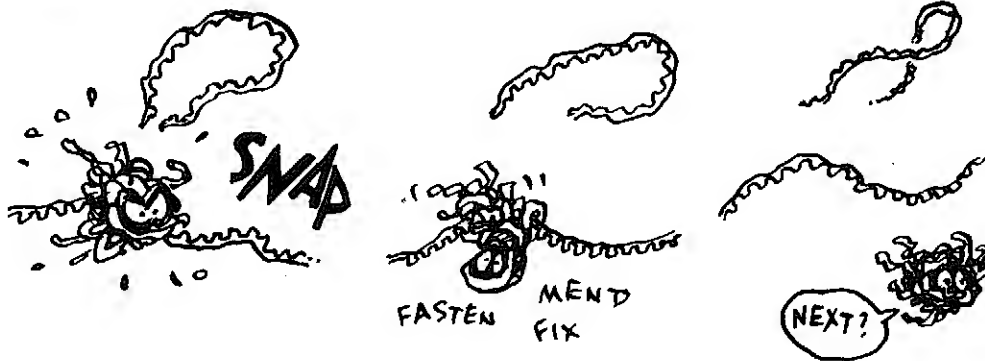


THE FUNCTION OF THESE AND OTHER ADJUSTMENTS TO EUKARYOTIC mRNA IS UNKNOWN.

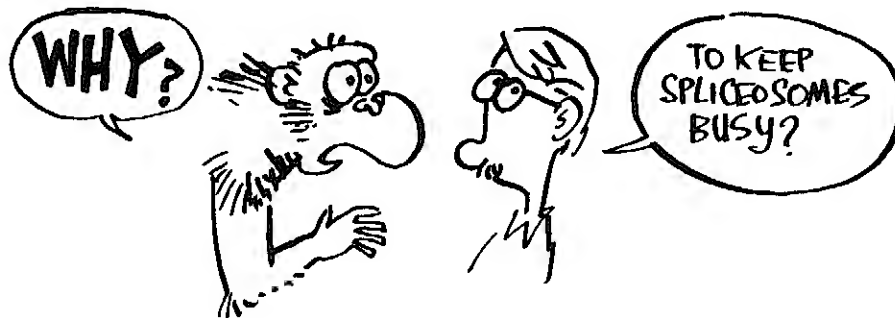
THE NEXT MOVE CAME AS A GREAT SURPRISE TO GENETICISTS:  
A COMPLEX OF PROTEIN AND RNA GRABS THE mRNA, FORMING  
LOOPS, LIKE THIS →



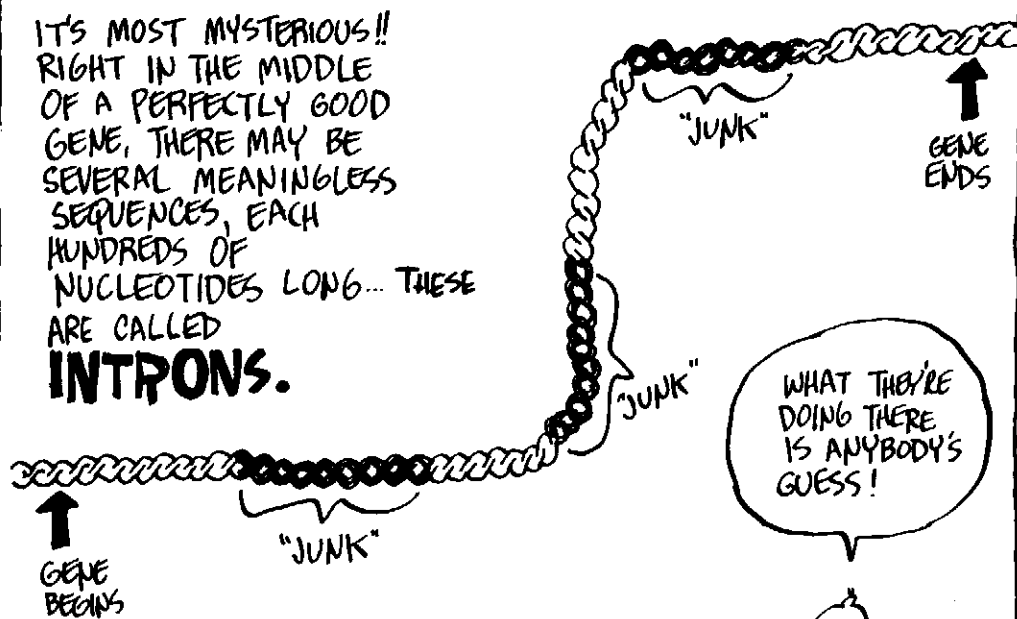
THE COMPLEX — CALLED A **SPLICEOSOME** —  
THEN SHEARS OFF THE LOOP, DISCARDS IT, SPLICES THE  
REMAINING PIECES TOGETHER, AND DEPARTS.



THIS IS BIZARRE! EUKARYOTIC GENES CONTAIN "**JUNK DNA**" —  
NON-CODING MESSAGE SEQUENCES THAT HAVE TO BE CUT OUT  
BEFORE THE GENE CAN BE EXPRESSED!!



IT'S MOST MYSTERIOUS!!  
RIGHT IN THE MIDDLE  
OF A PERFECTLY GOOD  
GENE, THERE MAY BE  
SEVERAL MEANINGLESS  
SEQUENCES, EACH  
HUNDREDS OF  
NUCLEOTIDES LONG... THESE  
ARE CALLED  
**INTRONS.**

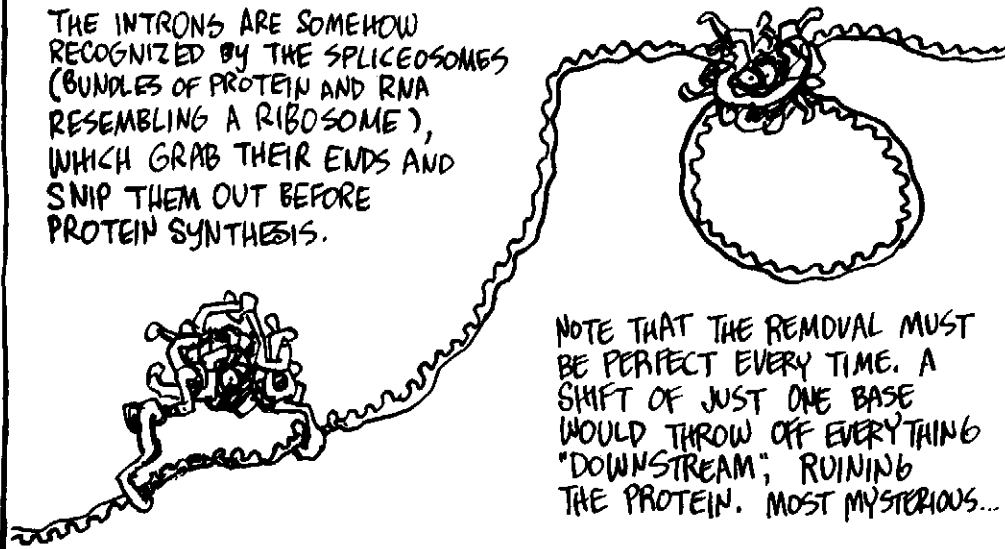


WHAT THEY'RE  
DOING THERE  
IS ANYBODY'S  
GUESS!



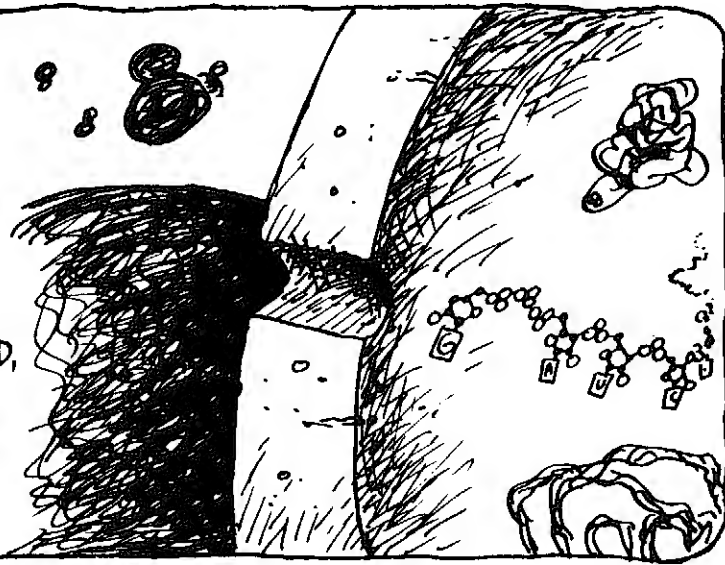
FOR SOME REASON, EUKARYOTES SEE  
FIT TO LEAVE INTRONS IN THE  
CHROMOSOME, ONLY REMOVING THEM  
FROM mRNA AFTER TRANSCRIPTION.

THE INTRONS ARE SOMEHOW  
RECOGNIZED BY THE SPLICEOSOMES  
(BUNDLES OF PROTEIN AND RNA  
RESEMBLING A RIBOSOME),  
WHICH GRAB THEIR ENDS AND  
SNIP THEM OUT BEFORE  
PROTEIN SYNTHESIS.

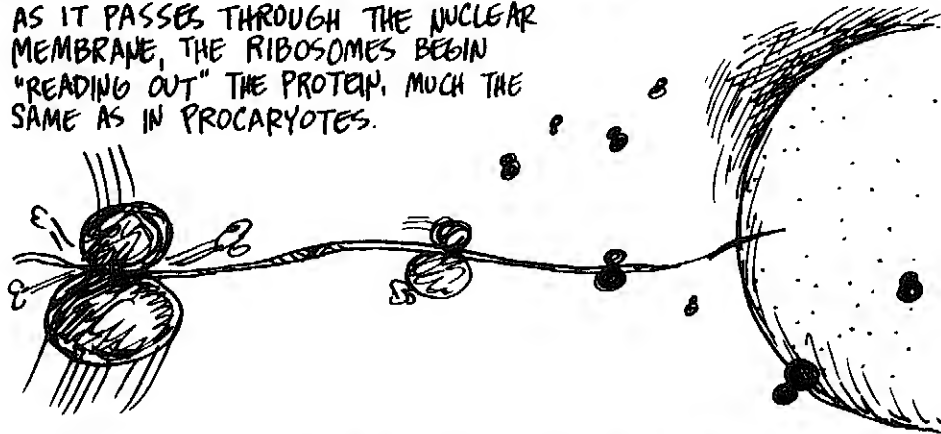


NOTE THAT THE REMOVAL MUST  
BE PERFECT EVERY TIME. A  
SHIFT OF JUST ONE BASE  
WOULD THROW OFF EVERYTHING  
"DOWNSTREAM", RUINING  
THE PROTEIN. MOST MYSTERIOUS...

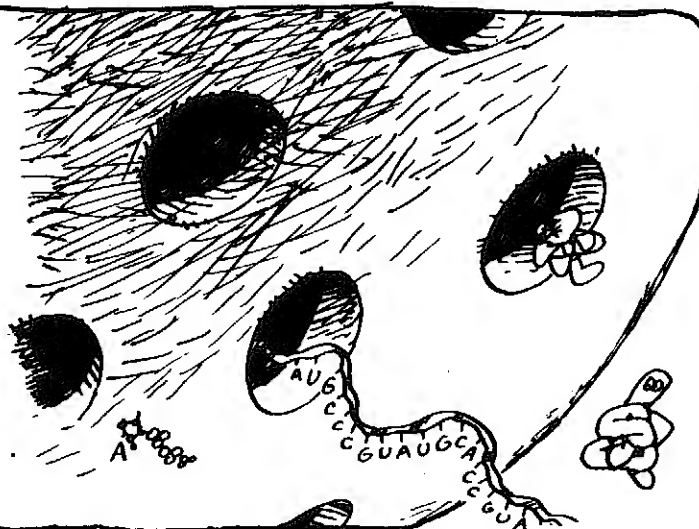
SO FAR,  
ALL THIS  
ACTION IS  
STILL TAKING  
PLACE INSIDE  
THE NUCLEUS,  
BUT NOW THE  
MESSENGER,  
SUITABLY CAPPED,  
TAILED, AND  
TRIMMED, IS  
READY TO  
GO...



AS IT PASSES THROUGH THE NUCLEAR  
MEMBRANE, THE RIBOSOMES BEGIN  
"READING OUT" THE PROTEIN, MUCH THE  
SAME AS IN PROCARYOTES.



FINALLY, THE  
PROTEIN GOES OFF  
TO DO ITS JOB;  
THE mRNA IS  
BROKEN DOWN  
INTO "SCRAP";  
AND THE PARTS  
RETURN TO  
THE NUCLEUS  
FOR RECYCLING,  
TOGETHER WITH  
THE ENZYMES  
THAT DO THE JOB.



# ANOTHER

DIFFERENCE BETWEEN EU AND  
A BACTERIUM IS IN THE SHEER  
NUMBER OF GENES: 200,000  
IN A HUMAN, 4000 IN E. COLI.



HMM... 200,000 GENES...  
1000 NUCLEOTIDES PER  
GENE... THAT'S 200  
MILLION... MY MY!

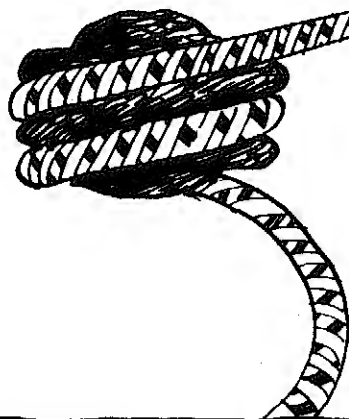
HA! I HAVE  
THAT MANY  
SISTERS LIVING  
IN YOUR GUT!



TO HELP ORGANIZE ALL  
THAT STORAGE, EUKARYOTES  
WRAP THEIR DNA AROUND  
PROTEIN "SPOOLS."  
EACH "SPOOL"—OR NUCLEOSOME  
CORE, TO BE PROPER—  
CONSISTS OF SEVERAL  
PROTEINS BOUND TOGETHER:



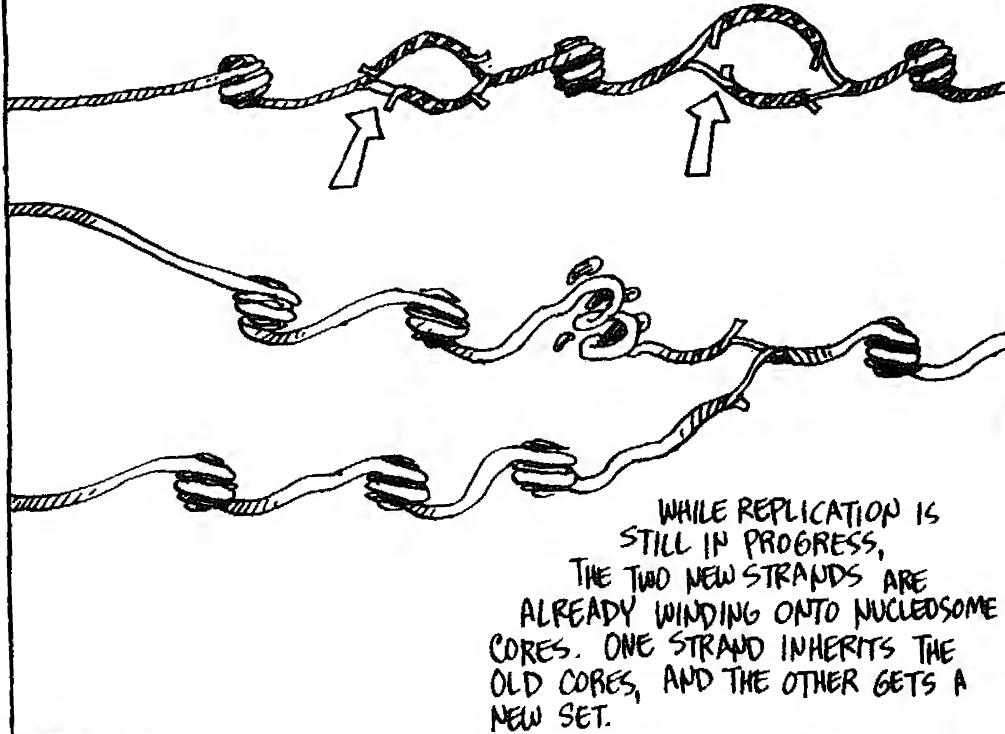
EACH CORE HAS A SPIRAL  
GROOVE FOR THE DNA,  
WHICH MAKES TWO  
TURNS AROUND IT.



HMM!  
VERY EXOTIC!

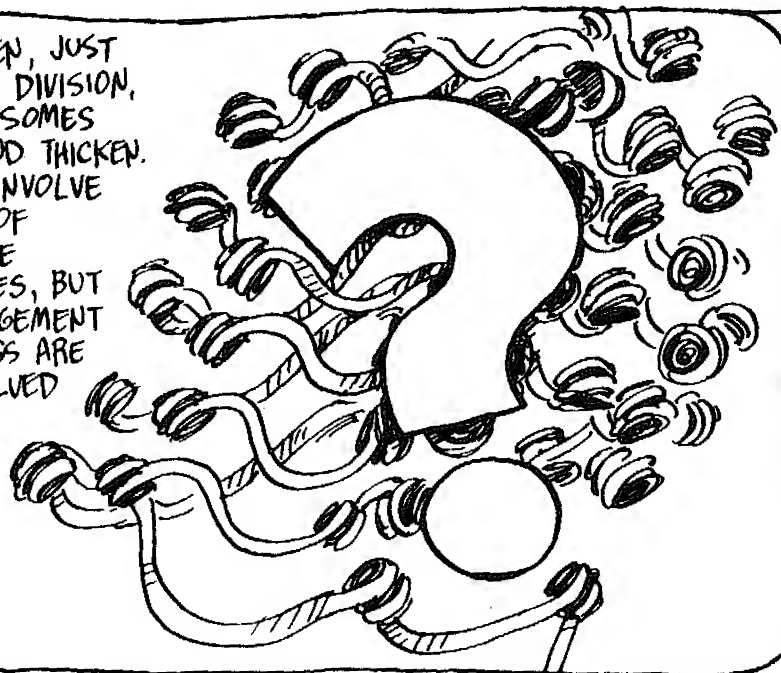


WHEN A EUKARYOTIC CELL WANTS TO DIVIDE, DNA REPLICATION BEGINS AT MANY SITES AT ONCE (UNLIKE IN E. COLI, WHERE IT BEGINS AT ONE SITE).

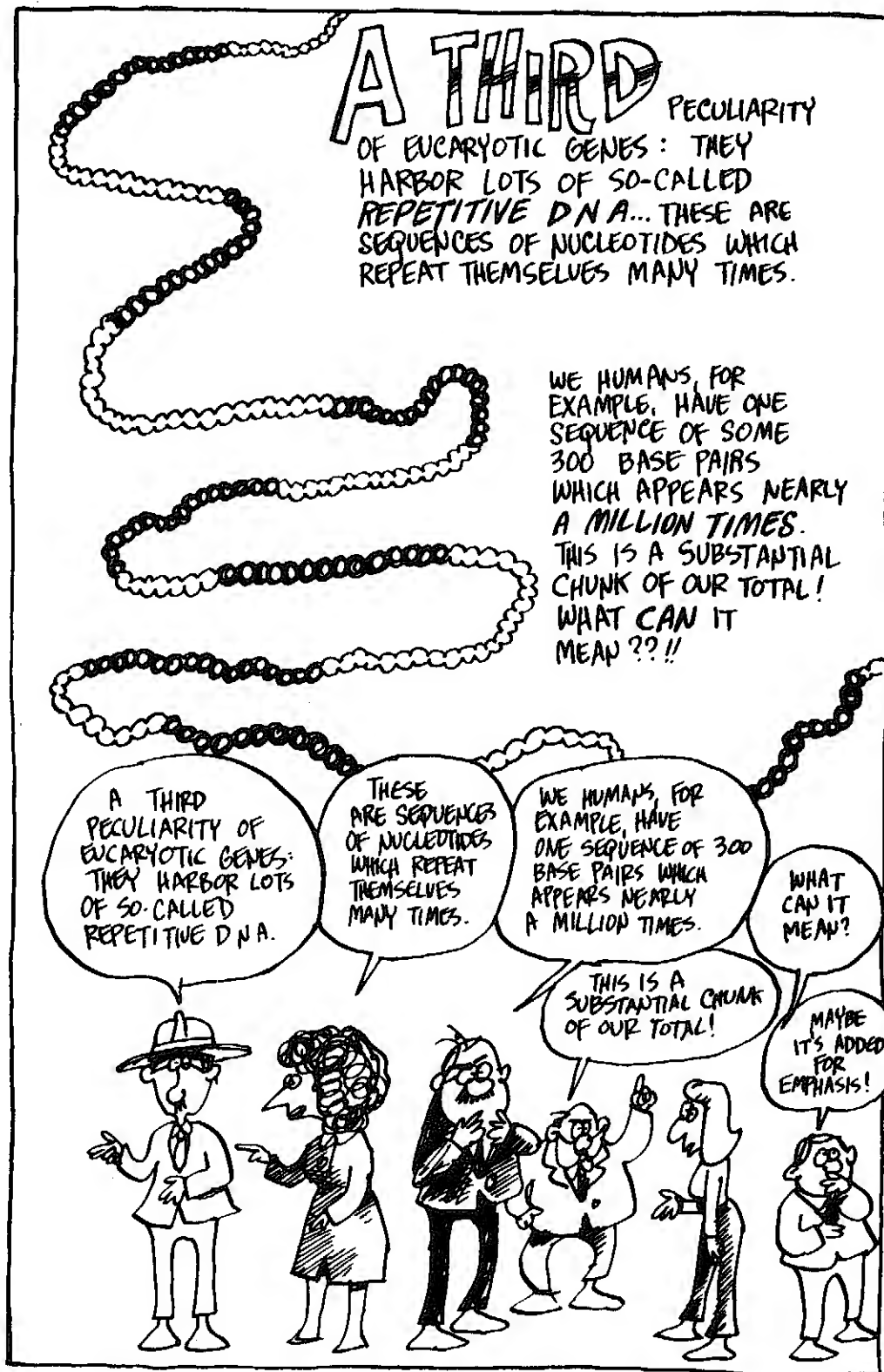


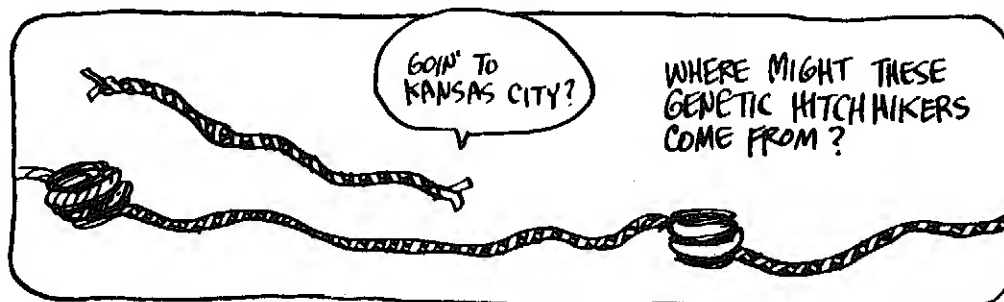
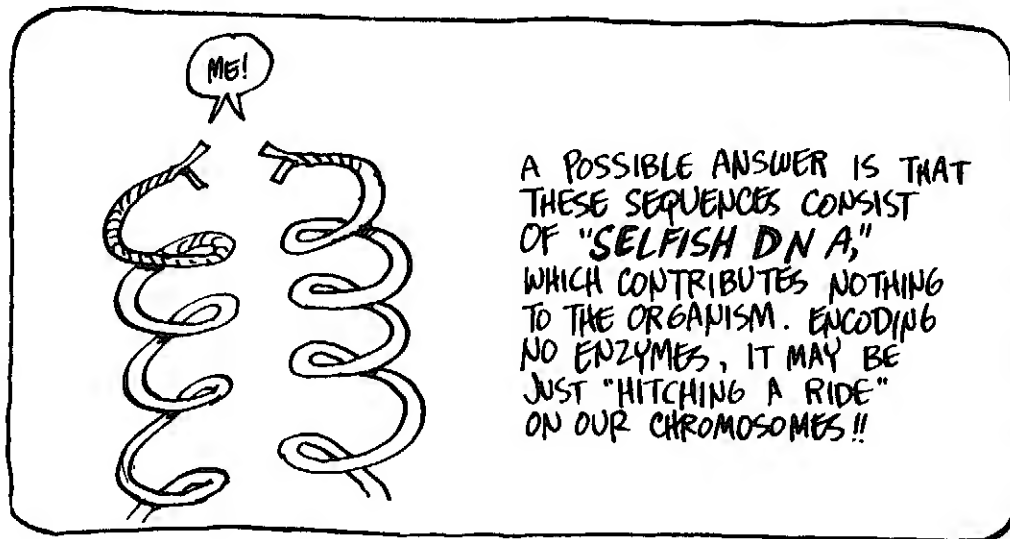
WHILE REPLICATION IS STILL IN PROGRESS, THE TWO NEW STRANDS ARE ALREADY WINDING ONTO NUCLEOSOME CORES. ONE STRAND INHERITS THE OLD CORES, AND THE OTHER GETS A NEW SET.

AS WE'VE SEEN, JUST BEFORE CELL DIVISION, THE CHROMOSOMES SHORTEN AND THICKEN. THIS MUST INVOLVE SOME WAY OF PACKING THE NUCLEOSOMES, BUT THE ARRANGEMENT AND PROCESS ARE STILL UNSOLVED PROBLEMS.



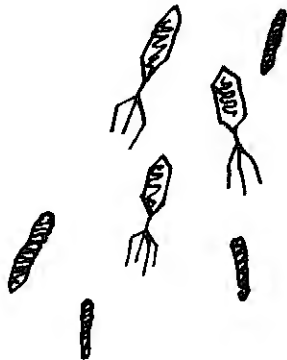






ONE POSSIBILITY IS  
THAT THEY COME FROM

# VIRUSES

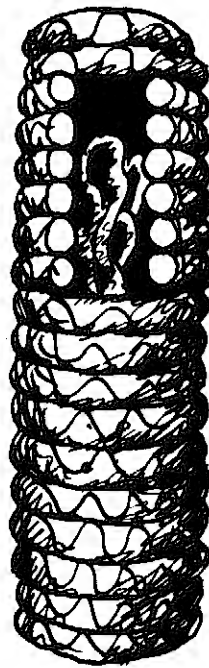


VIRUSES ARE THE SIMPLEST  
LIVING THINGS KNOWN—  
IF THEY'RE TRULY ALIVE AT  
ALL... THEY'RE SORT OF  
ALIVE AND NOT ALIVE...



REMINDS  
ME OF MY  
OLD  
BIOLOGY  
TEACHER...

EVEN SIMPLER AND SMALLER  
THAN A BACTERIUM, A  
VIRUS HAS ONLY TWO PARTS:  
A BIT OF NUCLEIC ACID  
WRAPPED UP IN A PROTEIN  
COAT:

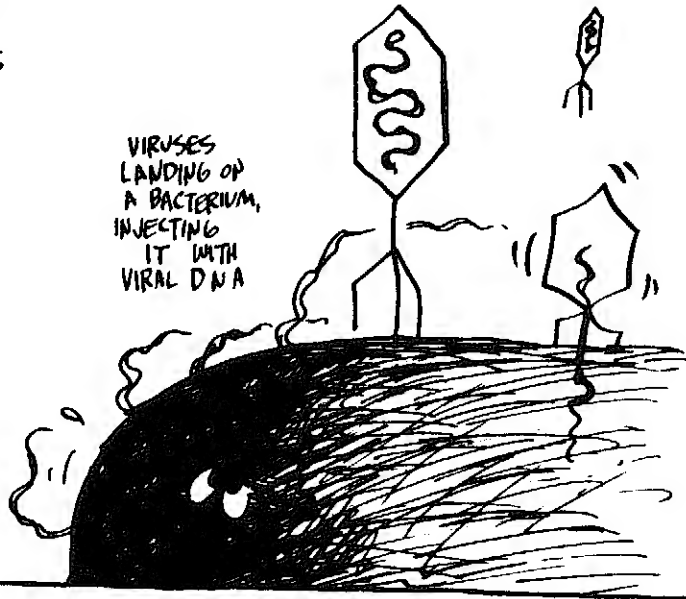


CUT-AWAY  
VIEW

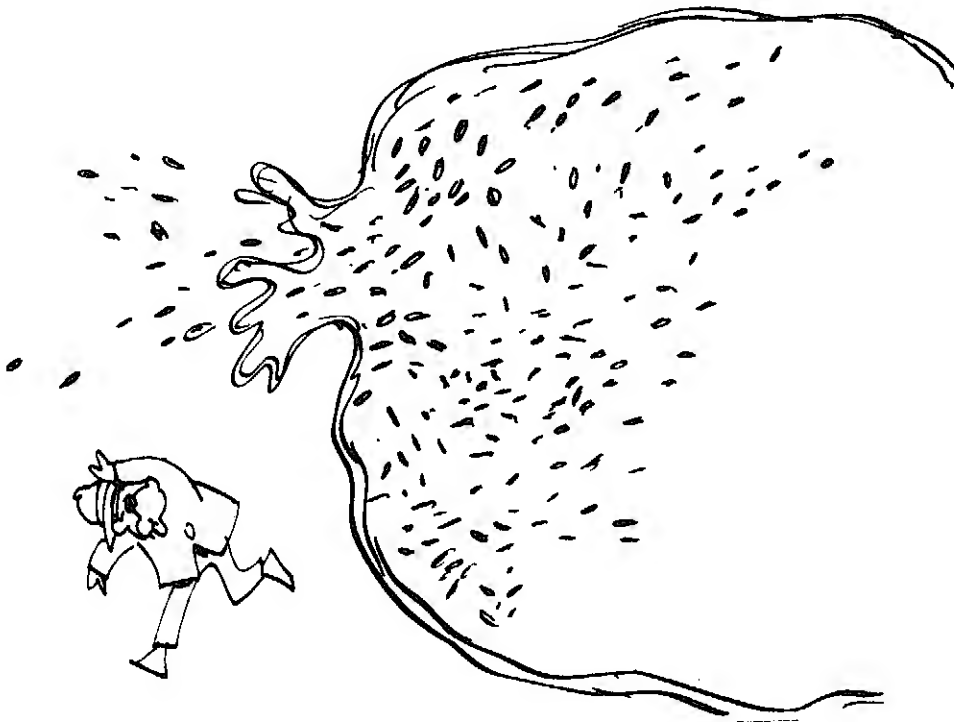
THE NUCLEIC  
ACID, WHICH  
MAY BE DNA  
OR RNA,  
ENCODES THE  
PROTEIN COAT  
AND A FEW  
ENZYMES  
NEEDED FOR  
REPLICATION.

BUT A VIRUS  
CAN'T REPRODUCE  
ON ITS OWN,  
BECAUSE IT LACKS  
RIBOSOMES AND  
THE REST OF  
A LIVING CELL'S  
PROTEIN-MAKING  
EQUIPMENT.  
A VIRUS CAN  
ONLY "LIVE" AS A  
PARASITE, BY  
INVADING A  
HOST CELL  
AND TAKING OVER  
ITS RIBOSOMES,  
ENZYMES, AND  
ENERGY.

VIRUSES  
LANDING ON  
A BACTERIUM,  
INJECTING  
IT WITH  
VIRAL DNA



ONCE IT GETS ITS DNA OR RNA INTO THE HOST, THE  
VIRUS BEGINS TO REPRODUCE WILDLY, STRAINING THE  
CELL TO THE BURSTING POINT!

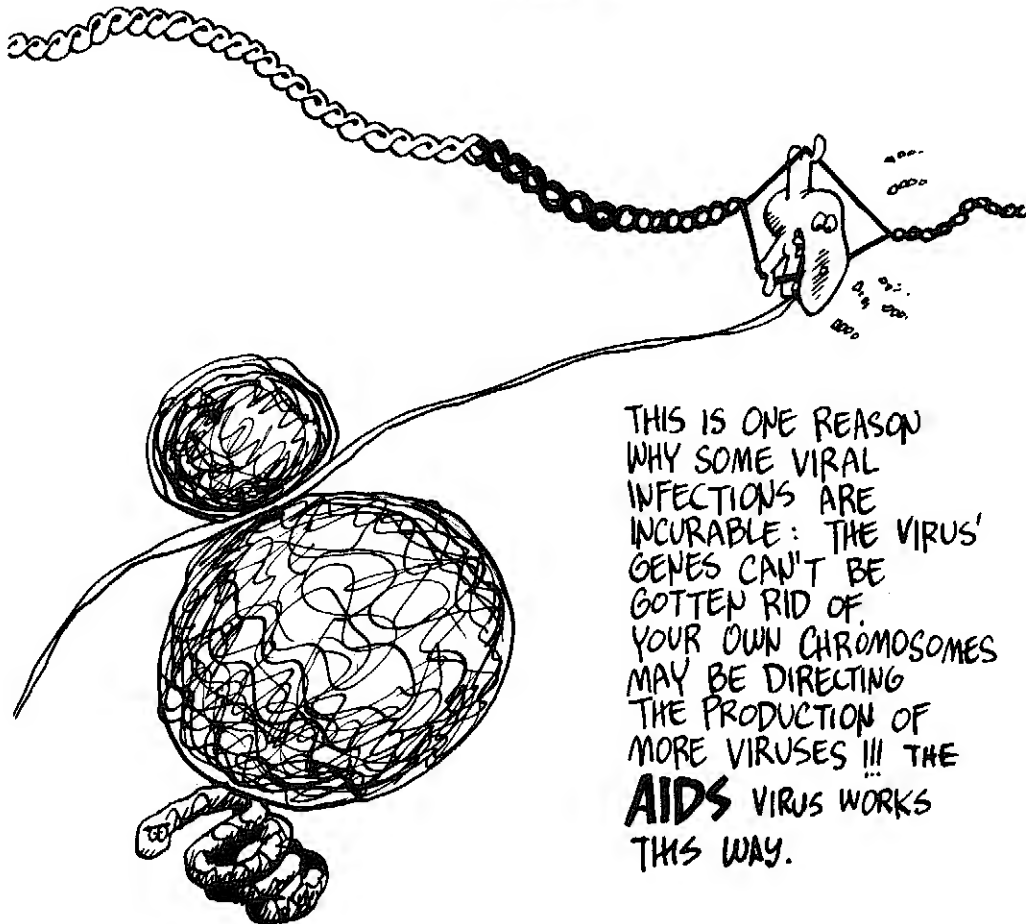
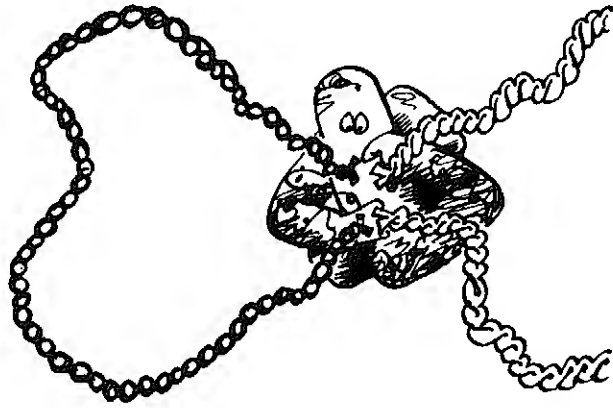


THAT'S A TYPICAL LIFE-STYLE (OR NON-LIFE-STYLE) FOR A VIRUS, BUT SOME VIRUSES ARE EVEN SNEAKIER: THEY ACTUALLY INSERT THEIR GENES INTO THE HOST CELL'S DNA.

---

## A RETRO- VIRUS

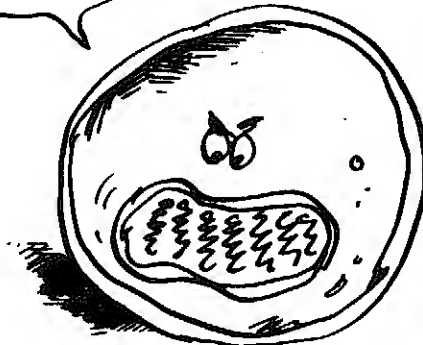
IS AN RNA VIRUS ENCODING AN ENZYME THAT MAKES A DNA COPY OF ITS RNA AND SPLICES IT INTO THE HOST CHROMOSOME.



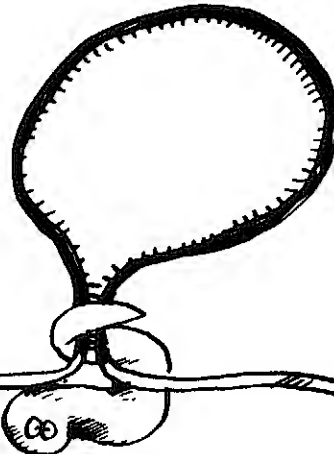
THIS IS ONE REASON WHY SOME VIRAL INFECTIONS ARE INCURABLE: THE VIRUS' GENES CAN'T BE GOTTEN RID OF. YOUR OWN CHROMOSOMES MAY BE DIRECTING THE PRODUCTION OF MORE VIRUSES !!! THE **AIDS** VIRUS WORKS THIS WAY.

IT'S POSSIBLE THAT SOME OF THE REPETITIVE AND "JUNK" DNA IN OUR CHROMOSOMES MAY HAVE COME FROM THIS SOURCE: ANCIENT VIRUSES THAT MANAGED TO INSERT THEIR HEREDITARY BLUEPRINT INTO OUR ANCESTORS' DNA.

SUBVERSIVE ELEMENTS!

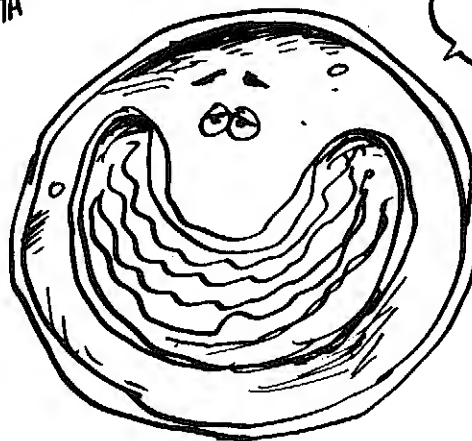


IF SO, THE "EDITING" OF mRNA MAY HAVE EVOLVED AS A DEFENSE AGAINST INAPPROPRIATE SEQUENCES STUCK INTO THE MIDDLE OF GENES.



THERE'S ANOTHER WAY A CELL CAN CONTEND WITH PARASITIC DNA: IT CAN SIMPLY SHUT THOSE GENES DOWN. THAT'S HOW WE DEAL WITH REPETITIVE SEQUENCES: THEY'RE THERE, BUT WE IGNORE THEM!

IT'S CALLED "REPRESSIVE TOLERANCE."



THE BATTLE AGAINST VIRUSES IS NEVER-ENDING...

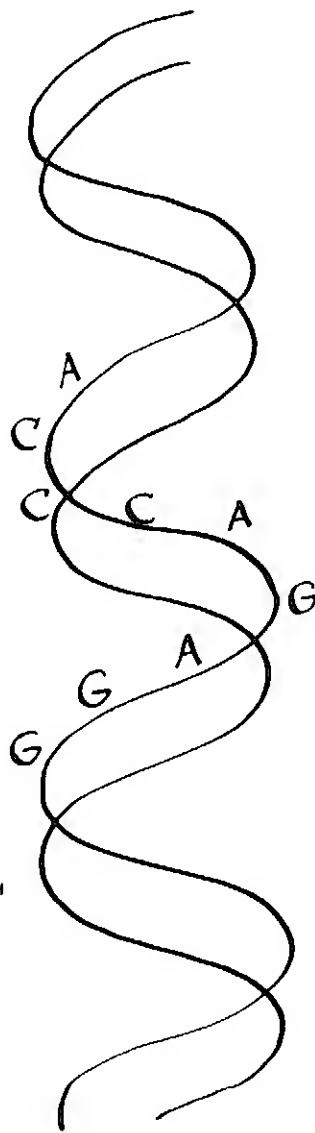
# Mutation & Dominance

(again!)

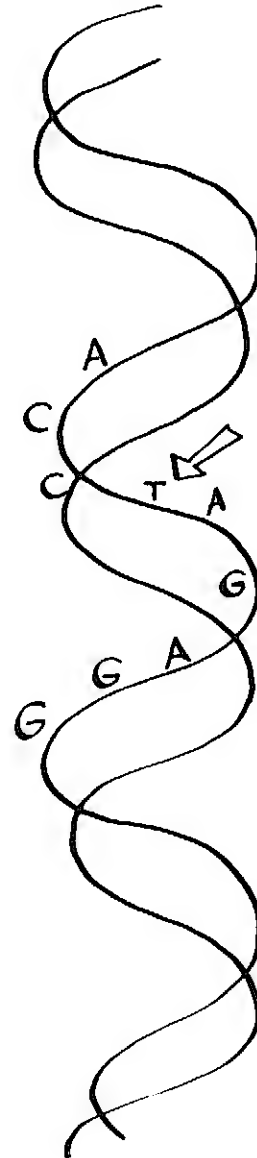
**N**OW THAT WE KNOW WHAT GENES REALLY ARE, WE CAN GET A MUCH BETTER GRASP OF MUTATION AND DOMINANCE.

A MUTATION IN A GENE IS JUST A CHANGE IN THE DNA'S SEQUENCE OF NUCLEOTIDES. EVEN A MISTAKE AT JUST ONE POSITION CAN HAVE A PROFOUND EFFECT.

HERE IS A SMALL BUT DEVASTATING MUTATION IN THE GENE FOR HEMOGLOBIN, THE PROTEIN WHICH CARRIES OXYGEN IN THE BLOOD.

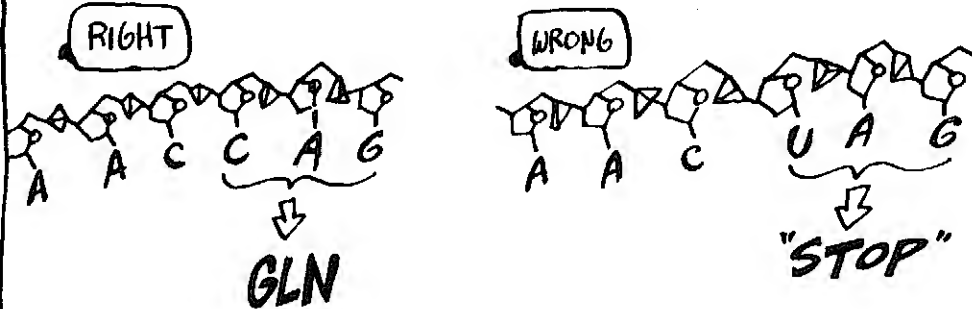


GOOD GENE



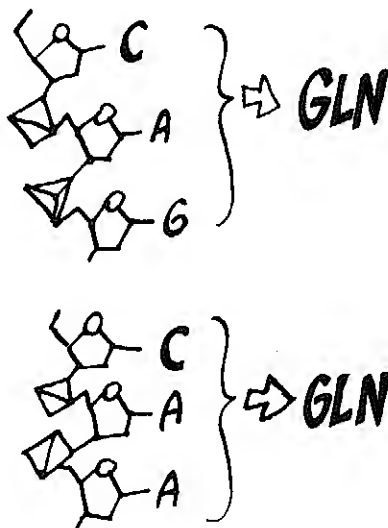
MUTANT GENE

THE REASON, OF COURSE, IS THAT THE CHANGE IS REFLECTED IN THE **PROTEIN** WHICH THE GENE ENCODES... FIRST THE mRNA COMES OUT WRONG, AND THEN THE PROTEIN...



THIS ESPECIALLY DISASTROUS MUTATION, WHICH INTERRUPTS THE PROTEIN IN THE MIDDLE, CAUSES A SERIOUS CONDITION CALLED **THALASSEMIA**, AN INABILITY TO MAKE HEMOGLOBIN. THE VICTIM SUFFERS FROM A PAINFUL LACK OF OXYGEN.

SOMETIMES A CHANGE MAY MAKE NO DIFFERENCE AT ALL. IF YOU REFER BACK TO THE CODE TABLE, YOU'LL RECALL THAT IT'S SOMEWHAT **REDUNDANT** — MEANING THAT ONE AMINO ACID MAY BE ENCODED BY SEVERAL DIFFERENT CODONS.





OCCASIONALLY, THE "MISTAKEN" AMINO ACID MAY FIT IN FAIRLY WELL (THOUGH USUALLY LESS THAN PERFECTLY).



SOMETIMES — ONCE IN A BLUE MOON — THE PROTEIN MAY EVEN WORK **BETTER** THAN BEFORE.



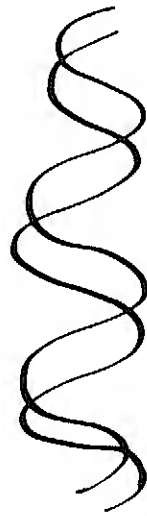
BUT MOST OF THE TIME, A MUTATION JUST RUINS THE PROTEIN. IT'S MUCH EASIER TO MESS SOMETHING UP THAN TO IMPROVE IT! IF YOU DOUBT IT, TRY MAKING RANDOM CHANGES IN SOME HOUSEHOLD APPLIANCE!!



## EARLIER (p. 81)

WE NOTED THAT MOST MUTATIONS ARE **RECESSIVE**. NOW WE CAN SEE WHY:  
A MUTATION USUALLY CAUSES AN **INABILITY** TO MAKE AN ENZYME. IN THE EXAMPLE ABOVE, THE MUTANT GENE FAILED TO MAKE HEMOGLOBIN.

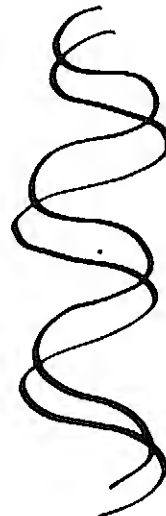
HOWEVER, WE HAVE TWO SETS OF CHROMOSOMES. EVEN IF A MUTATION AFFECTS ONE OF THEM, THE "INSURANCE" GENE WILL STILL PRODUCE ITS ENZYME.



GOOD GENE



HEMOGLOBIN



BAD GENE



NO HEMOGLOBIN

ONLY THE UNLUCKY SOUL WITH A DOUBLE DOSE OF MUTANT GENES WILL BE AFFLICTED WITH THALASSEMIA.



WHEN YOUR GENETIC INSURANCE LAPSES, THAT'S WHEN YOU'D BETTER GET MEDICAL INSURANCE!

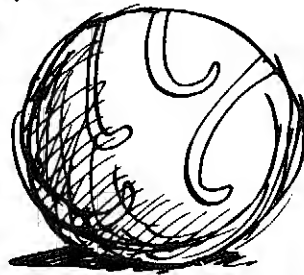
WE DIDN'T MENTION IT  
EARLIER, BUT SOME ALLELES  
CAN BE

# CO- DOMINANT,

MEANING THAT A  
HETEROZYGOTE MAKES  
BOTH PHENOTYPES.  
AN EXAMPLE IS BLOOD  
GROUPS.



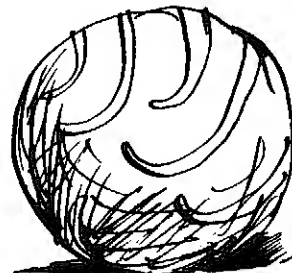
THERE IS A GENETICALLY  
DETERMINED SEQUENCE  
OF SUGARS LYING ON THE  
SURFACE OF RED BLOOD  
CELLS. ONE ALLELE,  $I^A$ ,  
MAKES SEQUENCE A.  
ANOTHER ALLELE,  $I^B$ ,  
MAKES SEQUENCE B.



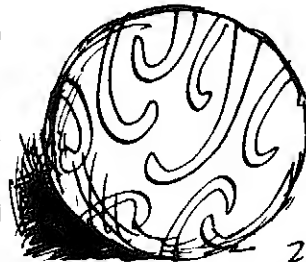
$I^A I^A$

IF HOMOZYGOUS FOR  
 $I^A$  YOUR BLOOD HAS  
ONLY SEQUENCE A.  
THIS IS TYPE A BLOOD.

$I^B I^B$



IF HOMOZYGOUS FOR  
 $I^B$ , YOU HAVE TYPE B  
BLOOD.



$I^A I^B$

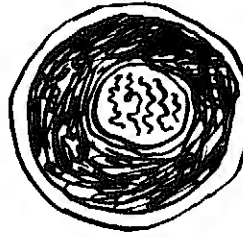
A HETERO-  
ZYGOTE MAKES  
BOTH SEQUENCES,  
AND HAS TYPE AB  
BLOOD.



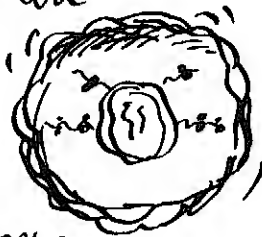
AND FINALLY, THERE  
IS A THIRD  
ALLELE,  $I^O$ , MAKING  
NO SUGAR  
SEQUENCE.  
TYPE O BLOOD IS  
RECESSIVE.



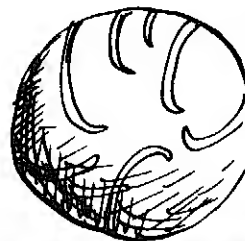
A RED BLOOD CELL BEGINS ITS EXISTENCE AS A BONE MARROW CELL, A PERFECTLY GOOD EUKARYOTE, BUT LACKING IN HEMOGLOBIN.



AT SOME POINT, A MARROW CELL BEGINS TO CHANGE... AMONG OTHER THINGS, IT BEGINS TO MAKE HEMOGLOBIN.



EVENTUALLY, IT EMERGES AS A

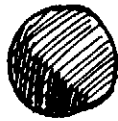


FULLY DEVELOPED RED BLOOD CELL.

GENETICALLY, THE POINT IS THIS: THE HEMOGLOBIN GENE WAS THERE ALL THE TIME, BUT IT WASN'T ALWAYS EXPRESSED—WHICH BRINGS US TO OUR NEXT SUBJECT...

# GENE REGULATION

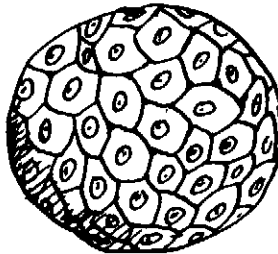
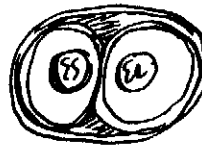
SORRY-  
YOU CAN'T  
PARK THAT  
GENE HERE-



ALL THE HIGHER LIFE  
FORMS EXHIBIT AN  
IMPRESSIVE COLLECTION OF  
CELL TYPES: NERVE,  
BLOOD, MUSCLE, SKIN, EYE,  
LYMPH, ETC ETC ETC...

**BUT**

DESPITE THEIR  
DIFFERENCES,  
ALL THESE  
CELLS HAVE  
PRECISELY  
THE SAME  
SET OF GENES\*,  
BECAUSE  
THEY ARISE  
FROM ONE  
FERTILIZED  
EGG BY  
THE PROCESS  
OF MITOSIS,  
WHICH  
DUPLICATES  
THE  
CHROMOSOMES.



\*AS USUAL, THERE ARE EXCEPTIONS !!

CLEARLY, DIFFERENT  
GENES COME  
INTO PLAY  
IN DIFFERENT  
CELLS... SO  
EACH CELL MUST  
HAVE WAYS  
OF "DECIDING"  
WHICH GENES  
TO "TURN ON"  
AND WHEN  
TO DO IT...



OTHERWISE,  
ONE DREADS  
THE RESULTS!

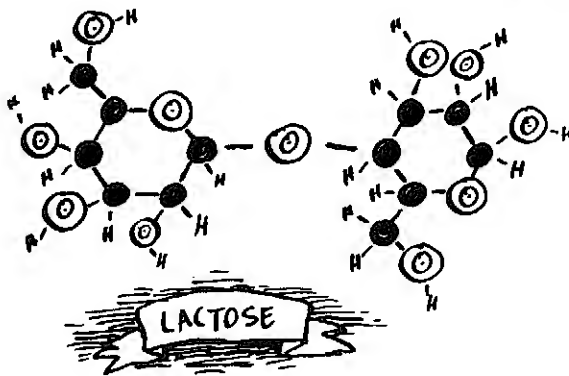
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EVEN THE LOWLY BACTERIUM NEEDS TO REGULATE ITS GENES.  
WHEN FOOD IS AVAILABLE, IT NEEDS TO MAKE ENZYMES TO  
DIGEST IT; WHEN IT RUNS LOW ON AN AMINO ACID, IT HAS  
TO SYNTHESIZE MORE; ETC ETC ETC...

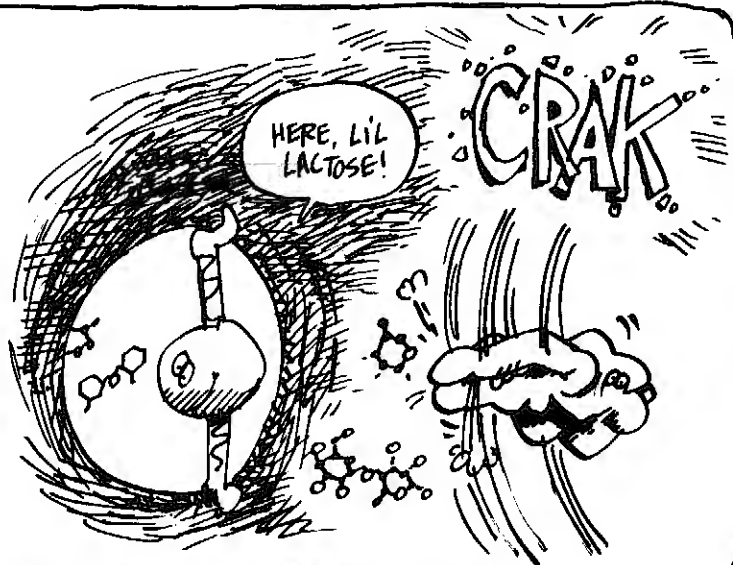


AS USUAL,  
THE QUESTION  
HAS BEEN  
MOST THOROUGHLY  
STUDIED IN  
E. COLI.

THE FIRST TO FIND A FORM OF GENE REGULATION WERE THE FRENCH SCIENTISTS JACQUES MONOD AND FRANÇOIS JACOB, IN THE LATE 1950'S. THEY EXAMINED *E. COLI*'S ABILITY TO DIGEST THE SUGAR LACTOSE.



IN THE PRESENCE OF LACTOSE, *E. COLI* PRODUCES TWO ENZYMES, CALL THEM Y AND Z\*. Z OPENS THE CELL WALL TO LACTOSE, AND Y BREAKS THE SUGAR IN HALF.



\* REAL NAMES: BETA-GALACTOSIDASE AND PERMEASE, RESPECTIVELY

WITHOUT GOING INTO THE DETAILS OF THEIR EXPERIMENTS, WHICH WERE QUITE INVOLVED, HERE ARE SOME OF MONOD AND JACOB'S MAIN RESULTS:

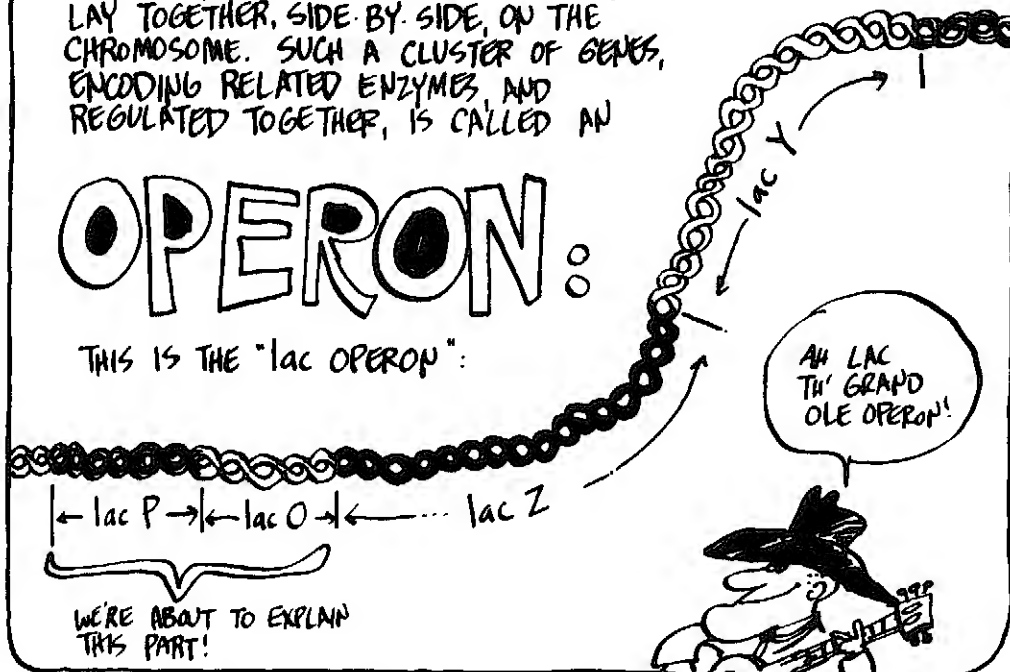


THIS EXPERIMENT WAS MORE DIFFICULT THAN A CHEESE SOUFFLÉ!

FIRST, THEY FOUND THAT THE GENES FOR Y AND Z, CALLED "lac Y" AND "lac Z," LAY TOGETHER, SIDE BY SIDE, ON THE CHROMOSOME. SUCH A CLUSTER OF GENES, ENCODING RELATED ENZYMES, AND REGULATED TOGETHER, IS CALLED AN

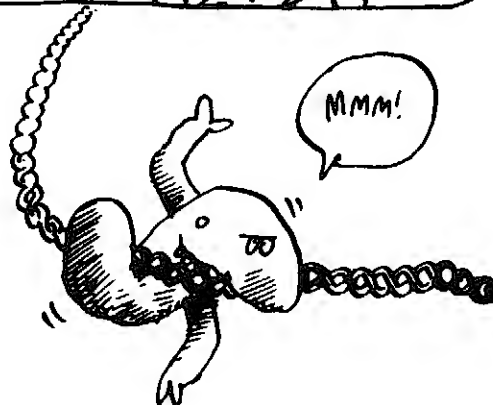
# OPERON:

THIS IS THE "lac OPERON":



WE'RE ABOUT TO EXPLAIN THIS PART!

AT THE START OF THIS (AND EVERY) OPERON IS A PROMOTER REGION, HERE CALLED lac P. THIS IS THE SITE WHERE THE ENZYME RNA POLYMERASE BINDS ONTO THE DNA TO BEGIN TRANSCRIBING THE MESSAGE INTO mRNA. (SEE p.133.)



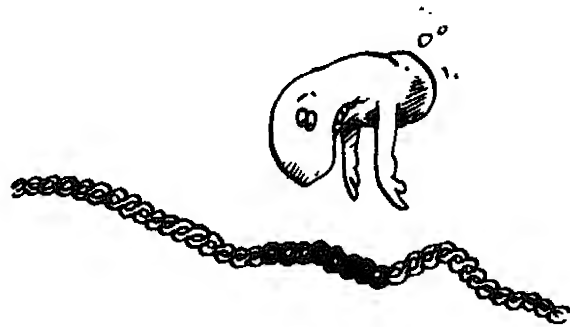


# The first

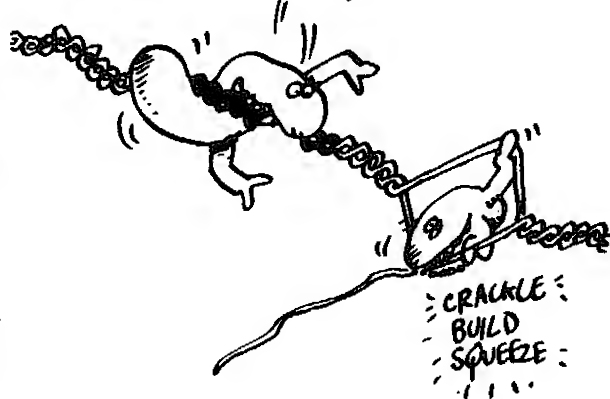
TYPE OF REGULATION IS SIMPLE:  
SOME PROMOTER REGIONS ARE MORE ATTRACTIVE TO RNA POLYMERASE THAN OTHERS.



THE GENE FOR A MUCH-USED ENZYME HAS A PROMOTER WHERE POLYMERASE MAY EASILY BEGIN TRANSCRIPTION, WHILE A GENE ENCODING AN ENZYME NEEDED IN SMALL AMOUNTS WILL HAVE A MORE "DIFFICULT" PROMOTER REGION.



"GLOW"



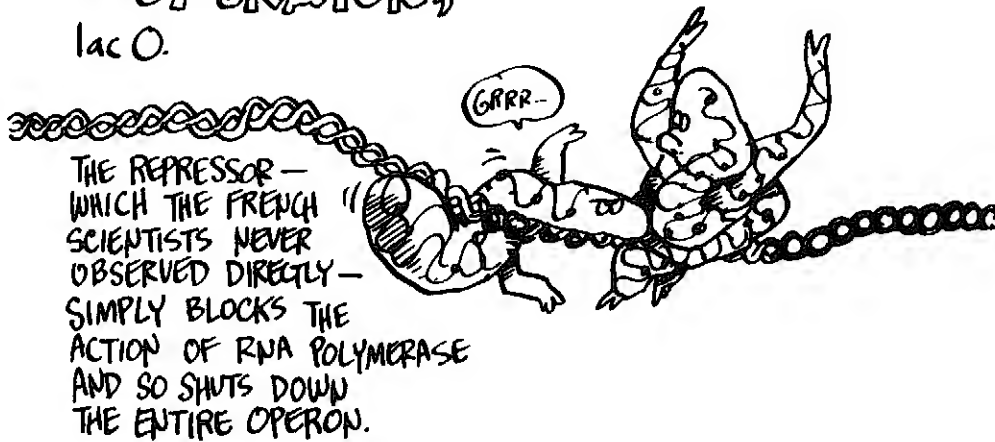
WHAT ABOUT THE LACTOSE OPERON, WHOSE ENZYMES ARE SOMETIMES NEEDED IN QUANTITY (WHEN LACTOSE IS PRESENT), BUT OTHERWISE NOT NEEDED AT ALL ??



MONOD + JACOB'S IDEA:  
THERE IS A PROTEIN,  
THE

# REPRESSOR,

WHICH SITS ON THE DNA  
AT A SPOT BETWEEN  
THE PROMOTER AND  
THE FIRST GENE, *lacZ*.  
THIS SPOT IS CALLED  
THE **OPERATOR**,  
*lacO*.



ONE MORE THING ABOUT THE REPRESSOR: IT CAN ALSO BIND  
TO **LACTOSE\***—BUT DOING SO CAUSES THE REPRESSOR TO  
“PLEX” AND RELEASE THE DNA:



\* ACTUALLY NOT LACTOSE ITSELF, BUT A DERIVATIVE SUBSTANCE — BUT NEVER MIND !!

IN THE NORMAL STATE OF AFFAIRS, THE REPRESSOR SITS ON THE OPERATOR, REPRESSING THE GENE:



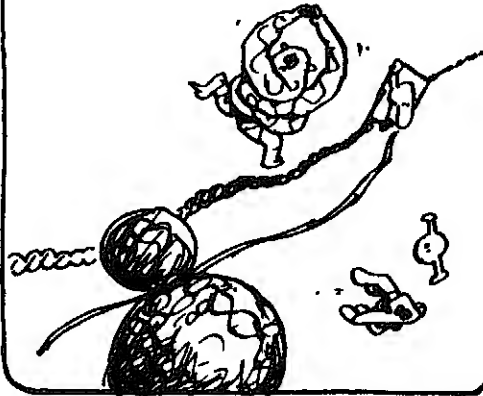
ALONG COMES A LITTLE LACTOSE, ATTRACTING THE REPRESSOR:



IT FLEXES, GRASPING THE SUGAR, AND RNA POLYMERASE SLIPS THROUGH!!



THE ENTIRE OPERON IS THEN EXPRESSED REPEATEDLY.



THE NEWLY MADE PROTEINS BRING IN MORE LACTOSE AND DIGEST IT...



FINALLY, WHEN ALL THE LACTOSE IS GONE, THE REPRESSOR UNFLEXES AND RETURNS TO ITS SPOT ON THE CHROMOSOME.

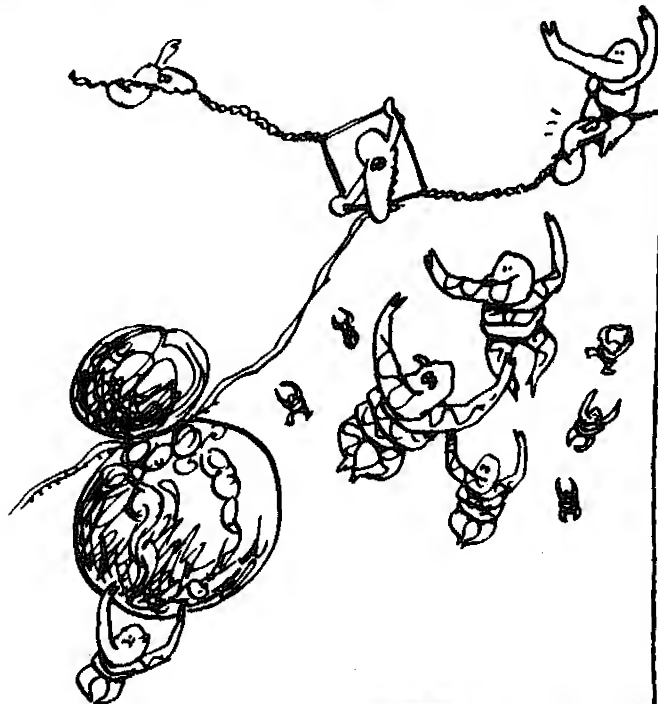


REPRESSORS  
TURN OUT TO BE  
A COMMON WAY  
TO REGULATE  
"INDUCIBLE" ENZYMES—  
I.E., ENZYMES WHICH  
ARE MADE IN  
RESPONSE TO A  
CHEMICAL-LIKE  
LACTOSE...  
BUT DESPITE THIS  
BRILLIANT IDEA,  
MONOD AND JACOB  
COULD NEVER  
ACTUALLY FIND A  
REPRESSOR. IT  
REMAINED A  
THEORETICAL POSSIBILITY...



...UNTIL 1967, WHEN WALTER GILBERT AND B. MÜLLER-HILL, USING  
VERY REFINED TECHNIQUES, WERE ABLE TO ISOLATE THE ELUSIVE  
PROTEINS.

THEIR RESULTS MADE  
PLAIN WHY IT  
HAD BEEN SO HARD  
TO FIND THEM:  
A SINGLE E. COLI  
BACTERIUM HAS  
ONLY FIVE TO  
TEN MOLECULES  
OF LAC REPRESSOR.  
LATER, GILBERT  
MANAGED TO  
BREED MUTANT  
E. COLI THAT  
PRODUCED IT  
IN MUCH LARGER  
AMOUNTS....



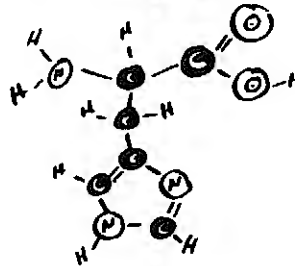
ANOTHER METHOD OF GENE  
REGULATION GOES BY THE NAME OF:

# ATTENUATION

AND ITS  
SUCCESSOR,  
ELEVEN-TUATION!

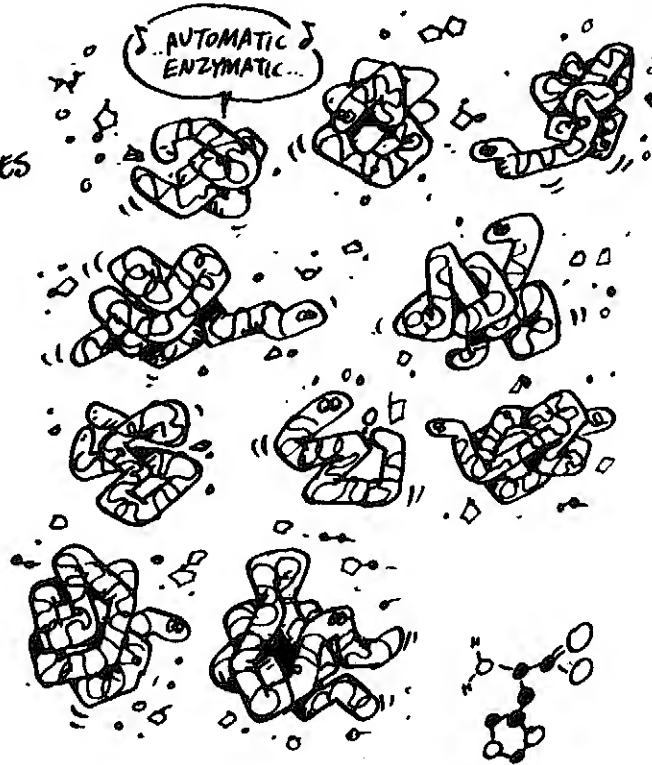


THIS GOVERNS AN E. COLI  
OPERON RESPONSIBLE FOR  
CONSTRUCTING THE AMINO  
ACID HISTIDINE.

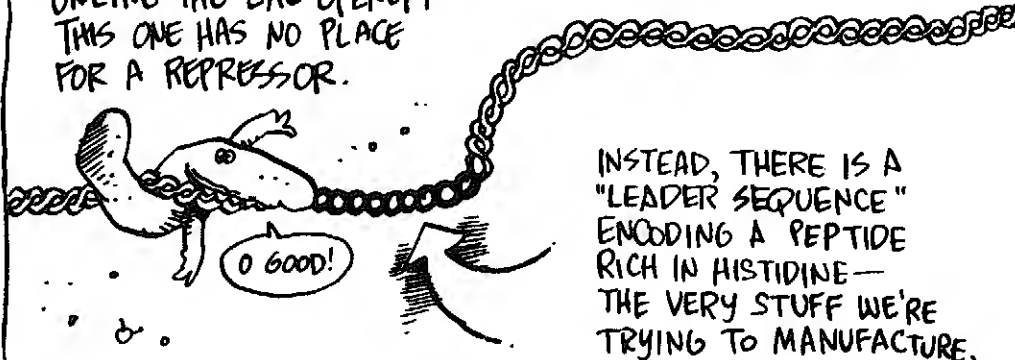


WHEN E. COLI  
RUNS LOW ON  
THIS ESSENTIAL  
STUFF THE  
BACTERIUM PRODUCES  
A GROUP OF  
NINE PROTEINS,  
WHICH CAN  
BUILD HISTIDINE  
MOLECULES  
FROM SCRATCH.

AN  
ENZYMATIC  
ASSEMBLY  
LINE!

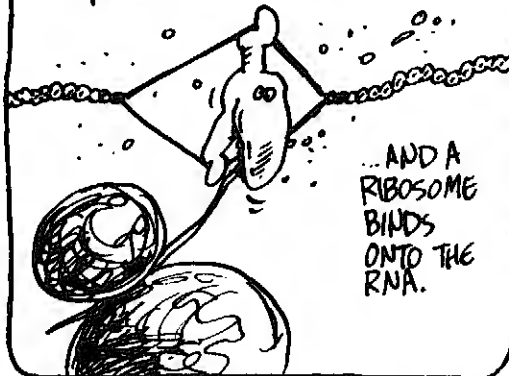


AS BEFORE, ALL 9 ENZYMES HAVE THEIR GENES CLUSTERED INTO AN OPERON, WITH AN INITIAL PROMOTER REGION. UNLIKE THE LAC OPERON, THIS ONE HAS NO PLACE FOR A REPRESSOR.

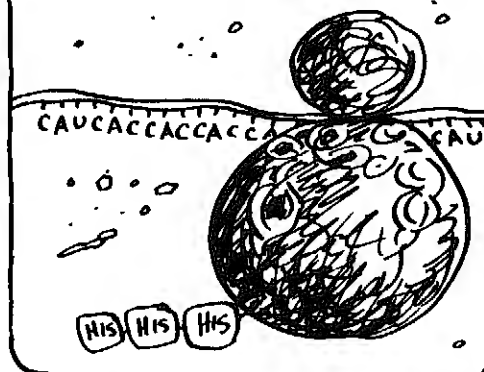


INSTEAD, THERE IS A "LEADER SEQUENCE" ENCODING A PEPTIDE RICH IN HISTIDINE—THE VERY STUFF WE'RE TRYING TO MANUFACTURE.

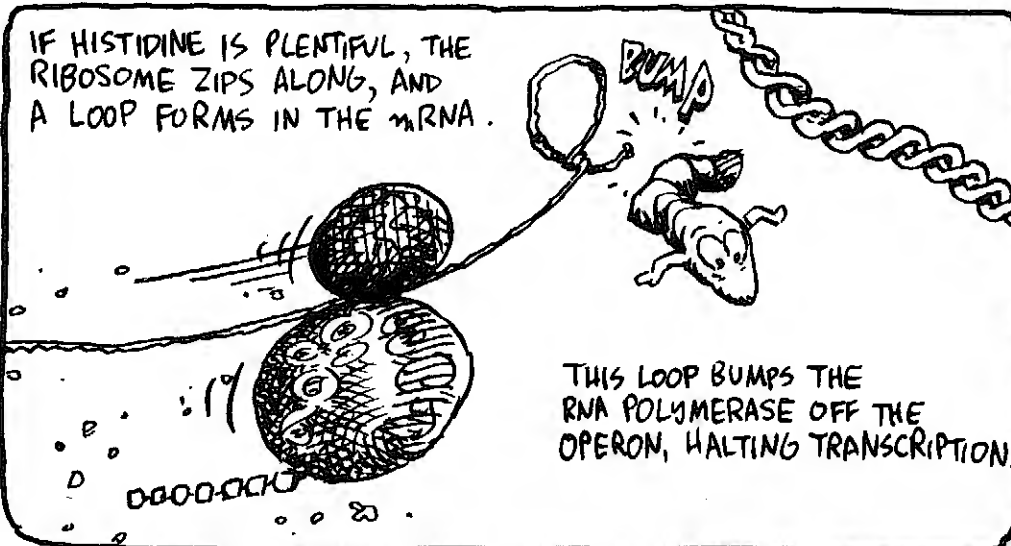
RNA POLYMERASE BEGINS BY TRANSCRIBING THE LEADER SEQUENCE...



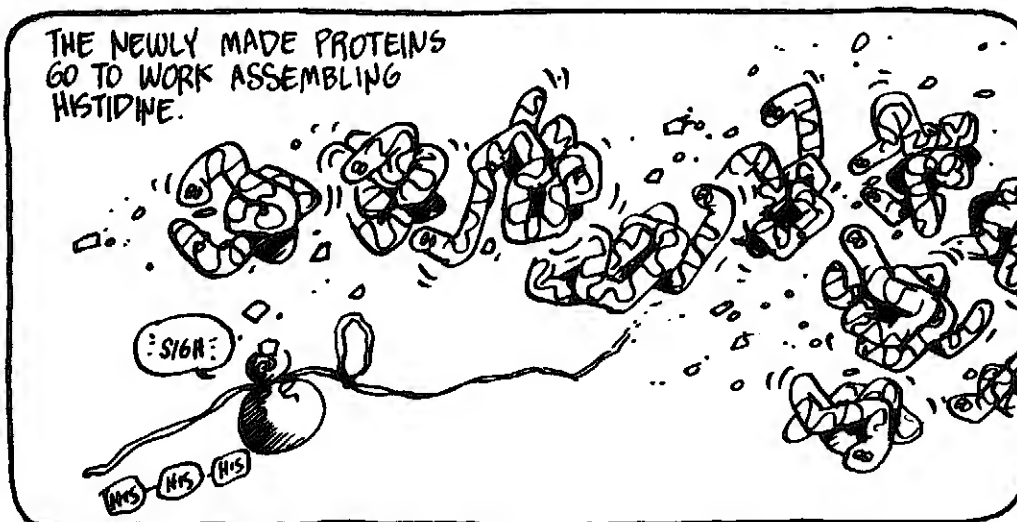
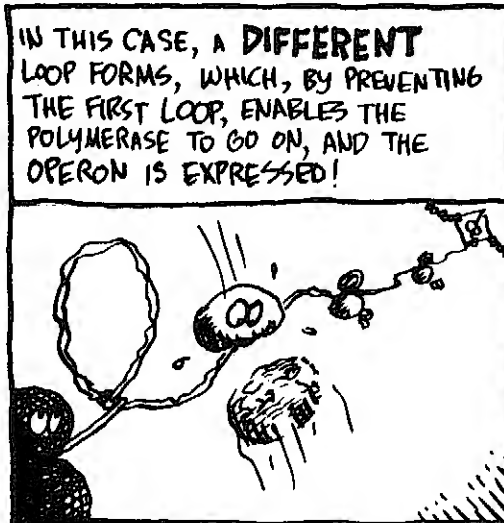
THE LEADER SEQUENCE ENCODES 7 HISTIDINES IN A ROW



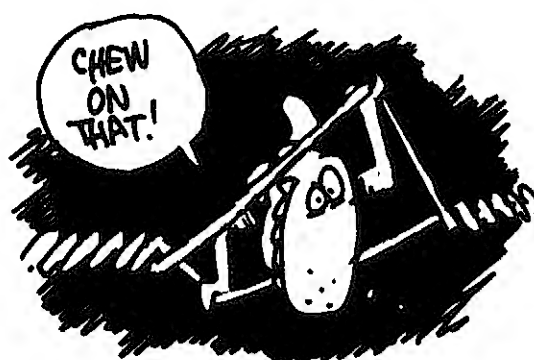
IF HISTIDINE IS PLENTIFUL, THE RIBOSOME ZIPS ALONG, AND A LOOP FORMS IN THE mRNA.



THIS LOOP BUMPS THE RNA POLYMERASE OFF THE OPERON, HALTING TRANSCRIPTION.



**RESULT?**  
A SHORTAGE OF HISTIDINE TURNS THE GENE ON, WHILE A HISTIDINE GLUT TURNS IT OFF.





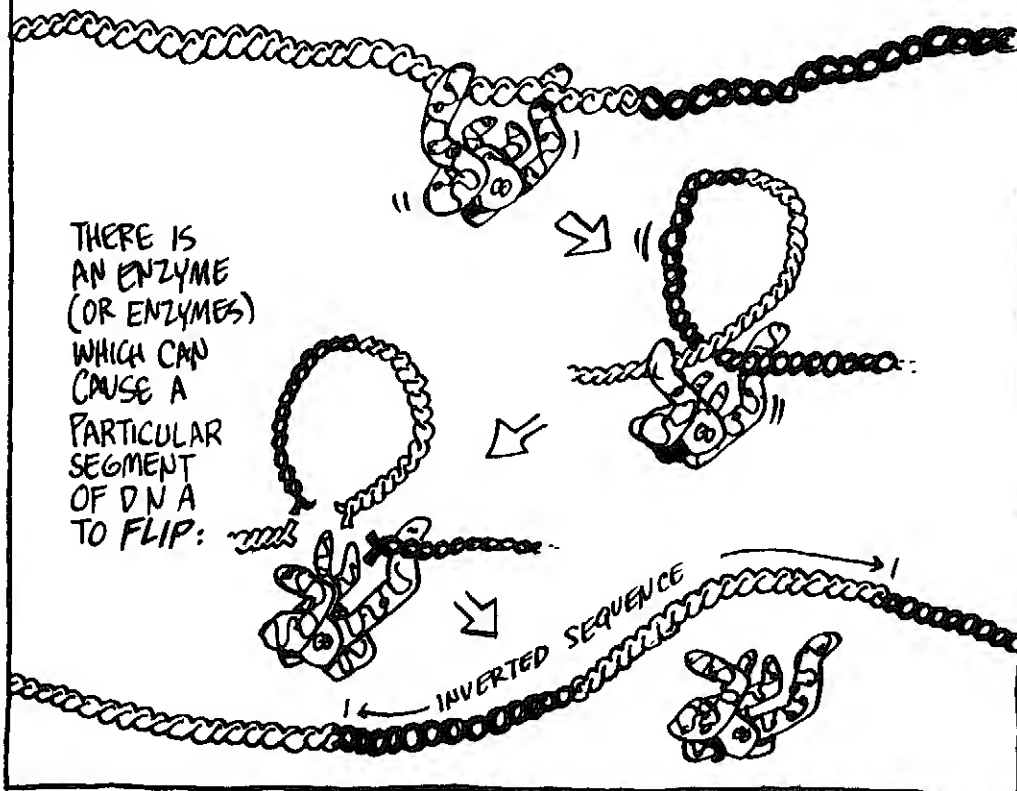
THE PORTRAIT OF THE GENE, AS SKETCHED BY MENDEL, AND FILLED IN BY LATER GENERATIONS, DEPICTED AN OBJECT FIXED AND UNCHANGING, ASIDE FROM OCCASIONAL MUTATIONS.

MORE RECENT DISCOVERIES SHOW A GENE MORE MOVABLE AND PLASTIC... IN FACT, AN IMPORTANT MEANS OF GENE REGULATION DEPENDS ON WHAT WE MIGHT CALL...

## JUMPING GENES.

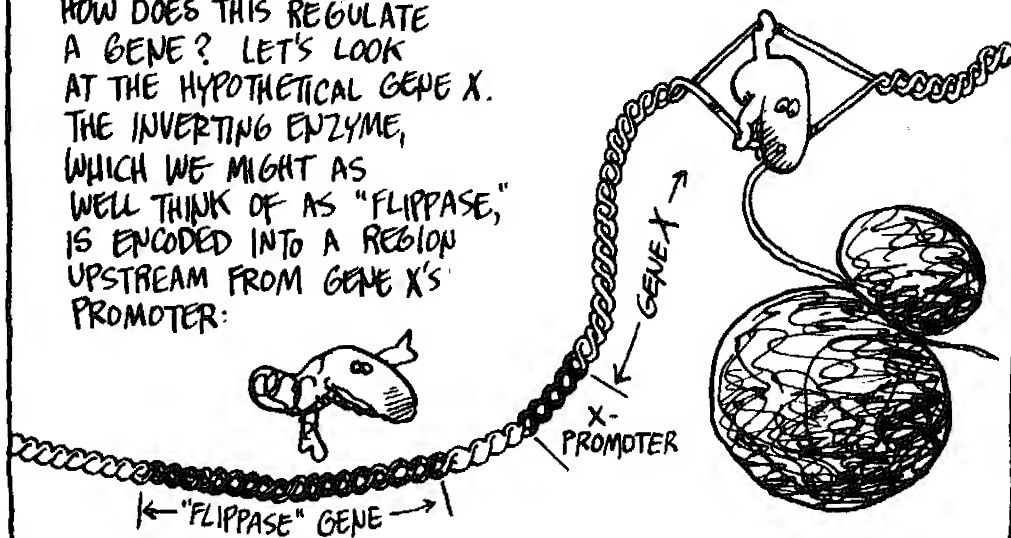


THERE IS AN ENZYME (OR ENZYMES) WHICH CAN CAUSE A PARTICULAR SEGMENT OF DNA TO FLIP:



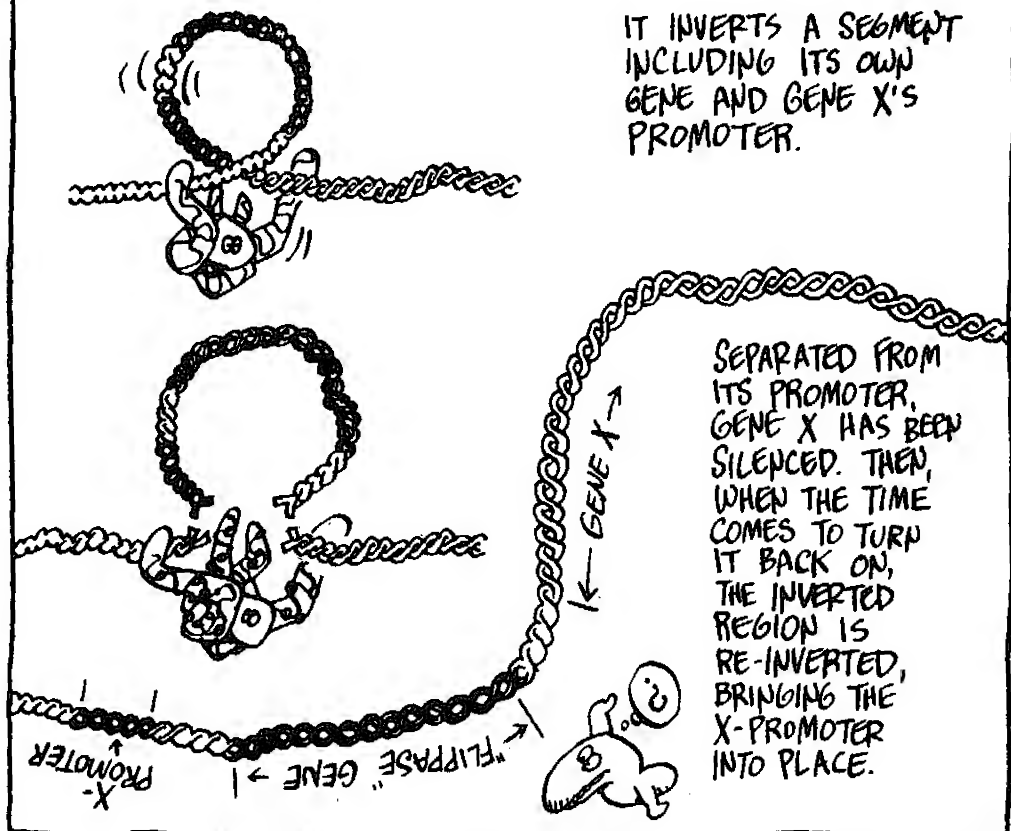


HOW DOES THIS REGULATE  
A GENE? LET'S LOOK  
AT THE HYPOTHETICAL GENE X.  
THE INVERTING ENZYME,  
WHICH WE MIGHT AS  
WELL THINK OF AS "FLIPPASE,"  
IS ENCODED INTO A REGION  
UPSTREAM FROM GENE X'S  
PROMOTER:



SOMEHOW, WHEN IT'S TIME TO SHUT OFF GENE X, THE  
FLIPPASE GENE IS ACTIVATED, MAKING THE ENZYME.

IT INVERTS A SEGMENT  
INCLUDING ITS OWN  
GENE AND GENE X'S  
PROMOTER.



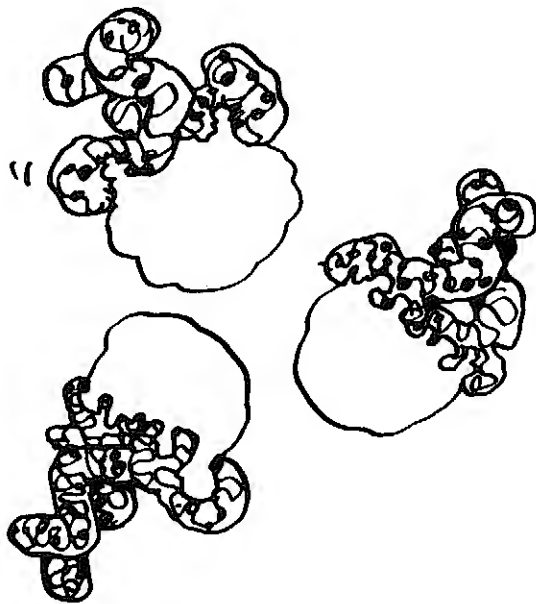
SEPARATED FROM  
ITS PROMOTER,  
GENE X HAS BEEN  
SILENCED. THEN,  
WHEN THE TIME  
COMES TO TURN  
IT BACK ON,  
THE INVERTED  
REGION IS  
RE-INVERTED,  
BRINGING THE  
X-PROMOTER  
INTO PLACE.

SUCH MOVABLE  
SECTIONS, OR  
**TRANSPOSONS,**

ARE COMMON IN BOTH  
PROCARYOTES AND  
EUCARYOTES. BESIDES  
INVERTING, THEY CAN  
JUMP FROM PLACE  
TO PLACE, FROM  
CHROMOSOME TO  
CHROMOSOME. THE  
FULL FUNCTION OF  
TRANSPOSONS IS  
STILL A MYSTERY.



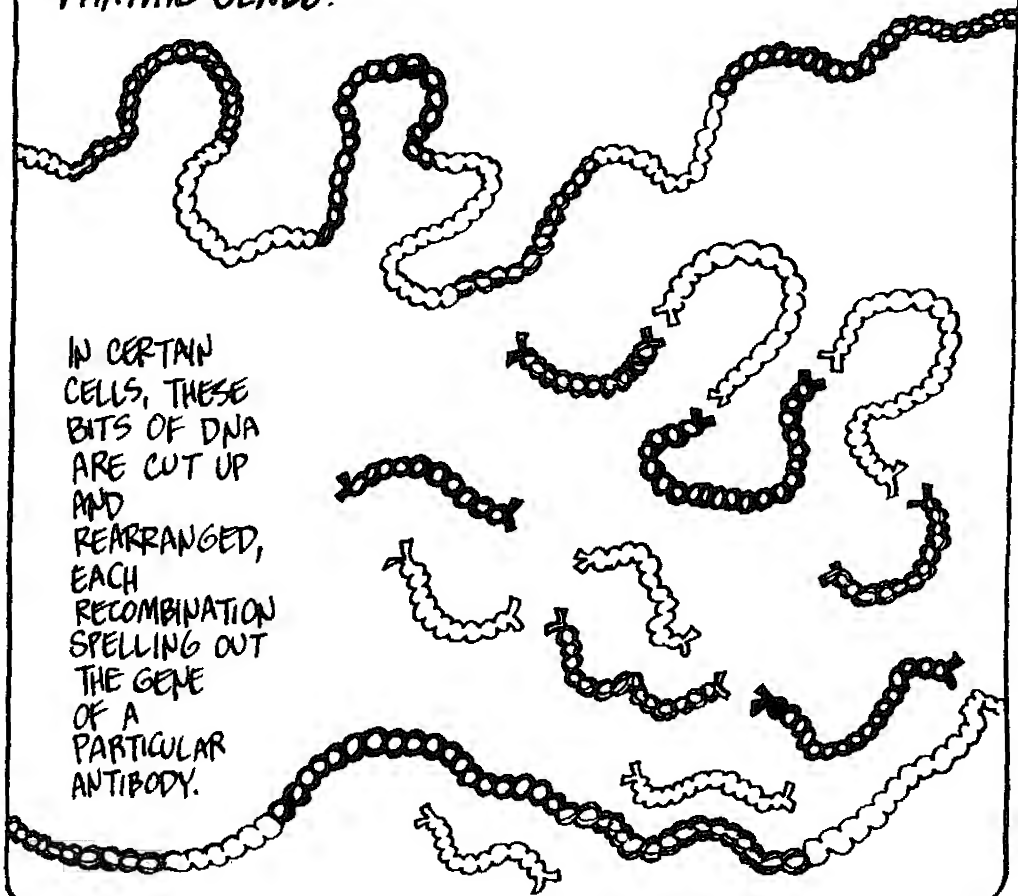
THE MOST SPECTACULAR EXAMPLES OF JUMPING GENES ARE  
THE ONES ENCODING ANTIBODIES.



ANTIBODIES ARE  
PROTEINS WHICH  
SERVE AS THE BODY'S  
DEFENSIVE WEAPONS.  
THEY ATTACK  
BACTERIA, VIRUSES,  
AND OTHER  
HARMFUL INVADERS.  
THERE ARE LITERALLY  
BILLIONS OF  
POTENTIAL ANTIBODIES,  
EACH KEYED TO  
THE EXACT SHAPE  
OF ITS "ENEMY."  
HOW CAN SO MANY  
BE ENCODED IN  
GENES?

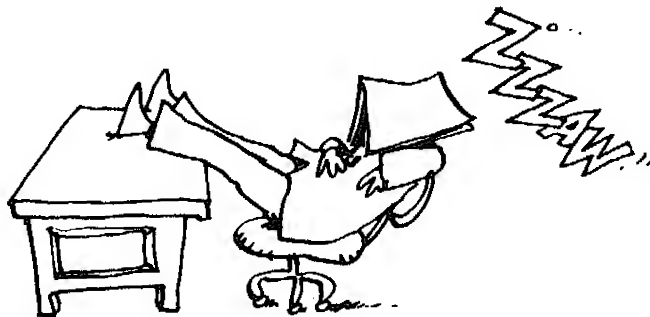
RATHER THAN HAVING BILLIONS OF GENES FOR ANTIBODIES, THE CHROMOSOMES CARRY A "TOOL KIT" OF A FEW HUNDRED PARTIAL GENES.

IN CERTAIN CELLS, THESE BITS OF DNA ARE CUT UP AND REARRANGED, EACH RECOMBINATION SPELLING OUT THE GENE OF A PARTICULAR ANTIBODY.



HOW THE ORGANISM REGULATES THIS PROCESS IS STILL A RIDDLE, AS ARE MOST MATTERS OF EUKARYOTIC GENE REGULATION: THE QUESTION OF HEMOGLOBIN (P. 163), FOR EXAMPLE, REMAINS WITHOUT AN ANSWER.

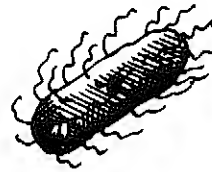
IT'S CLEAR THAT THE FLEXIBLE GENES OF EUKARYOTES WILL BE AN ACTIVE AREA OF RESEARCH IN YEARS TO COME.



# GENETIC ENGINEERING

LIVING CELLS ARE  
NOT THE ONLY ONES  
CAPABLE OF REARRANGING  
GENES!! NOW SCIENTISTS  
TOO HAVE THE POWER...

... A GREATER POWER  
THAN BIOLOGISTS  
HAVE EVER KNOWN...



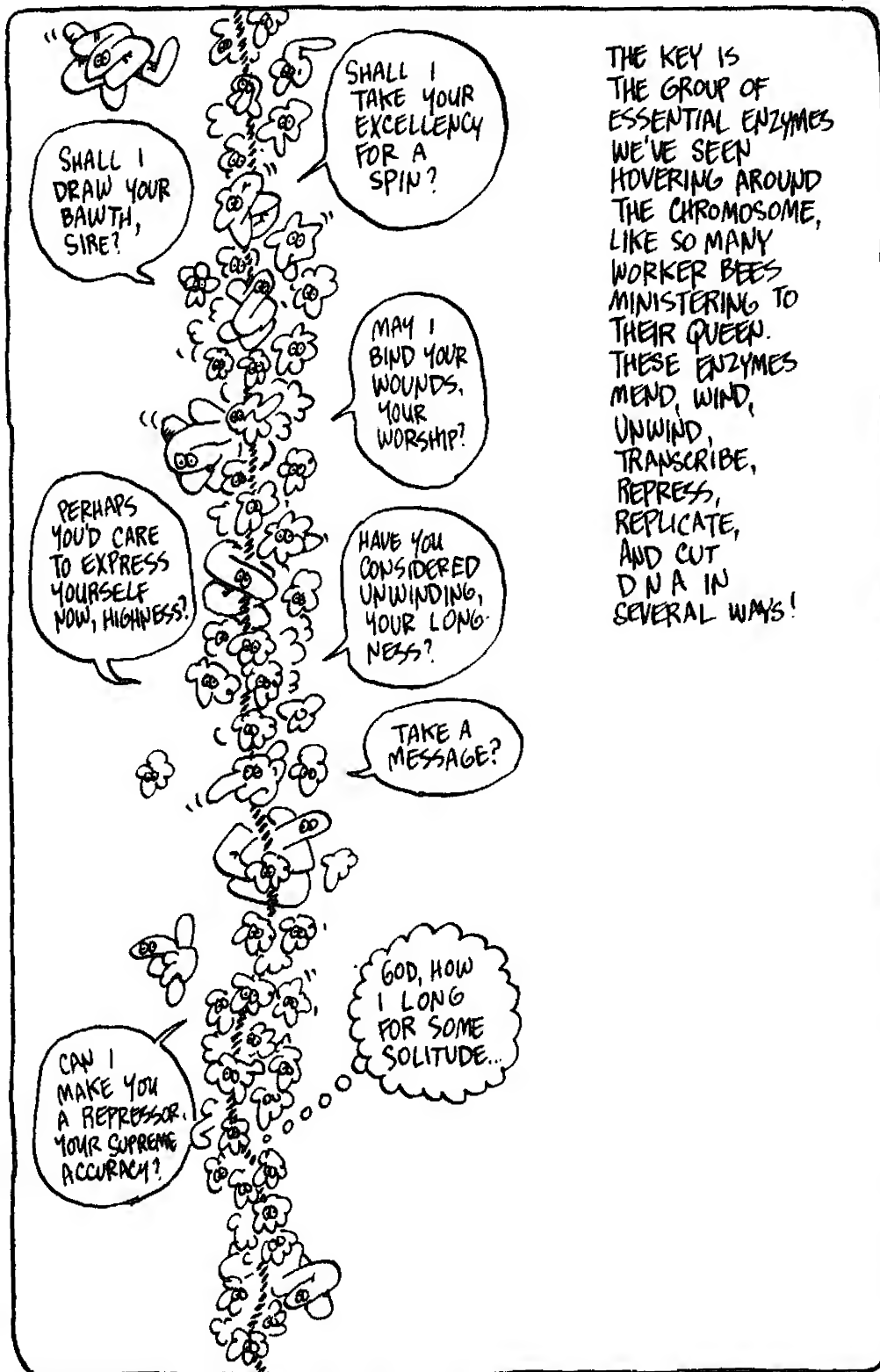


THE COMBINATIONS CAN BE PRETTY BIZARRE: MOST COMMONLY, HUMAN GENES ARE ATTACHED TO THOSE OF A BACTERIUM, LIKE *E. COLI*...



THIS IS WHAT  
YOU CALL

**RECOMBINANT  
DNA**



GENE SPLICING DEPENDS  
ON A SPECIAL TYPE OF  
CUTTING ENZYME  
CALLED A **RESTRICTION  
ENDONUCLEASE**, OR  
RESTRICTION ENZYME  
FOR SHORT.

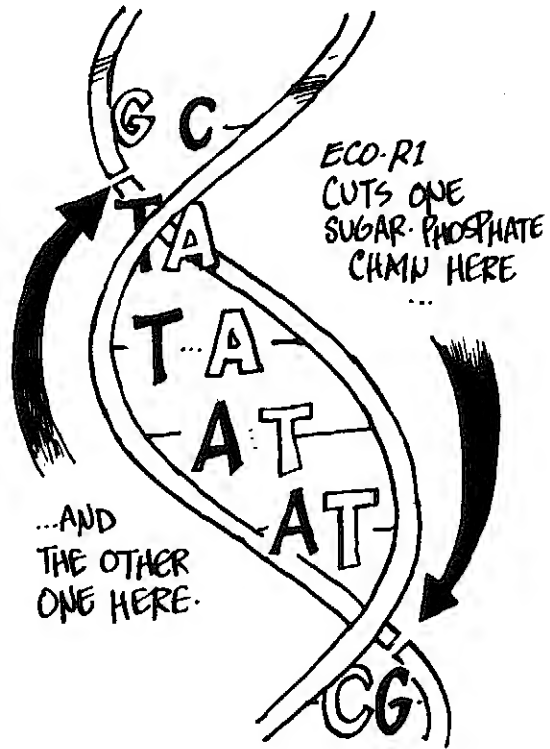
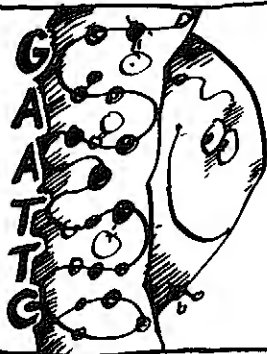


A RESTRICTION  
ENZYME  
MAKES A  
"STAGGERED  
NICK"  
IN DNA  
AT A  
SPECIFIC  
SEQUENCE  
OF BASES.



THE ENZYME **ECO. R1**,  
FOR EXAMPLE, RECOGNIZES  
ONLY THE SEQUENCE

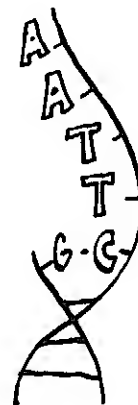
-G-A-A-T-T-C-  
: : : :  
-C-T-T-A-A-G-



**ECO. R1**  
CUTS ONE  
SUGAR-PHOSPHATE  
CHAIN HERE  
...

...AND  
THE OTHER  
ONE HERE.

THIS CREATES TWO PIECES  
OF DNA WITH IDENTICAL  
T-T-A-A "TAILS." (BECAUSE  
C-T-T-A-A-G IS THE SAME AS  
ITS COMPLEMENT READ  
BACKWARDS!)



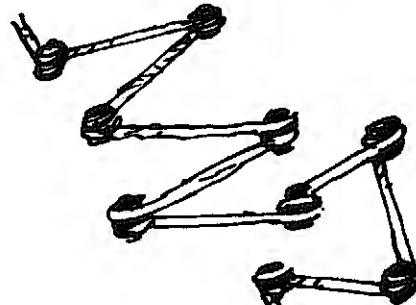
E. COLI USES  
ECO-R1 TO  
CHOP UP  
"ENEMY" VIRAL  
DNA,  
BUT HUMANS  
HAVE PUT  
IT TO  
CONSTRUCTIVE  
USE.

YOU'RE  
BEATING  
MY SWORDS  
INTO  
FLOWSHARES?

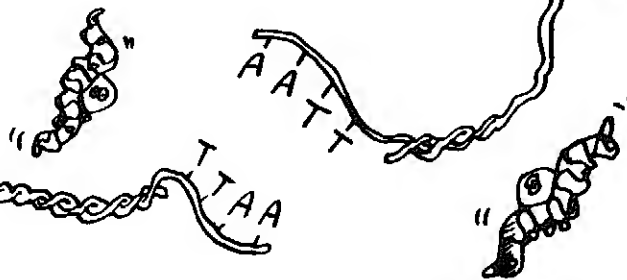
NO... STOCK SHARES  
IN GENETIC ENGINEERING  
COMPANIES..



THEY BEGIN WITH DNA FROM TWO DIFFERENT SOURCES, SAY  
E. COLI AND HUMAN, AND TREAT BOTH WITH ECO-R1 IN THE  
SAME TEST TUBE.

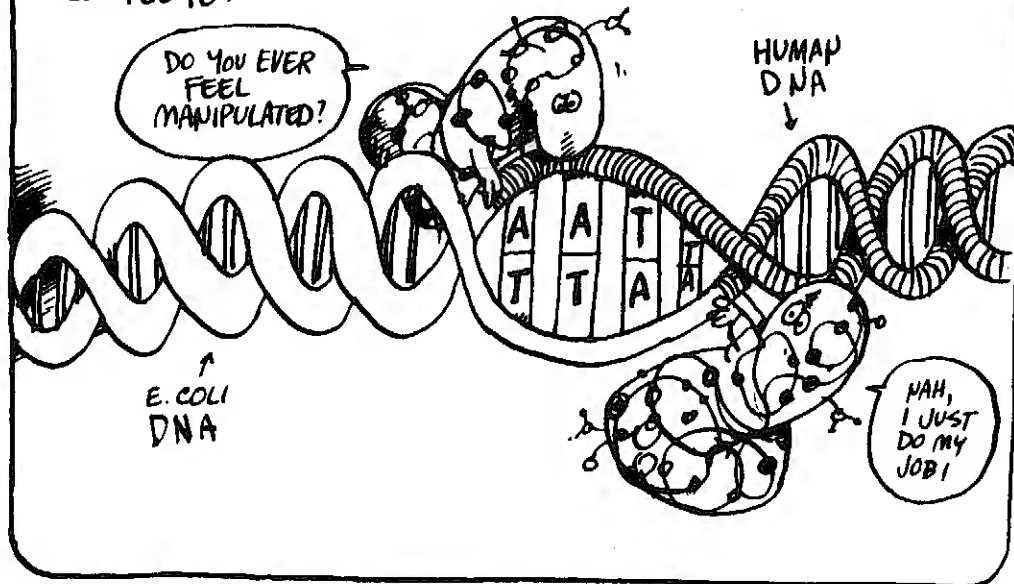


THIS GIVES THEM BOTH  
THE "SELF-BACKWARDS-  
COMPLEMENTARY" TAIL,  
T-T-A-A.





THE TAILS SNAP TOGETHER, AND, AFTER TREATMENT WITH **LIGASE**, AN ENZYME THAT SEALS NICKS IN THE SUGAR-PHOSPHATE CHAIN, THE **RECOMBINANT DNA** IS COMPLETE!



WHAT CAN YOU DO WITH THIS HYBRID MOLECULE? WHAT HAPPENS WHEN RECOMBINANT DNA IS INSERTED INTO A LIVING SYSTEM? UNDER SOME CONDITIONS, IT TURNS OUT THAT GENE SPLICING CAN BE USEFUL IN PRACTICE...

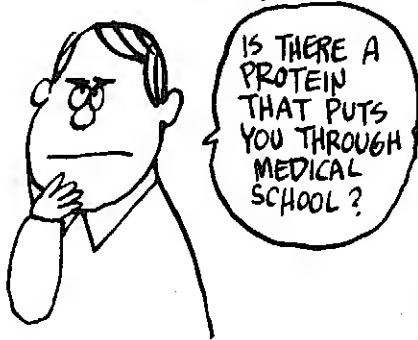


THE TECHNIQUE IS CALLED

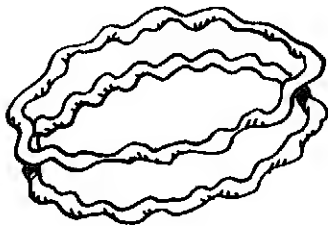
# GENE CLONING

AND IT WORKS LIKE THIS:

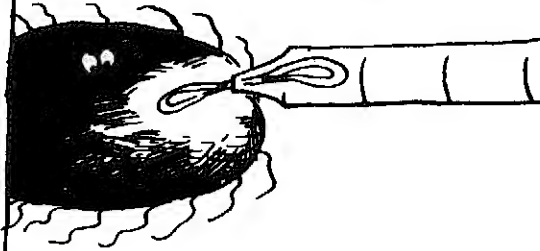
FIRST, CHOOSE A HUMAN GENE ENCODING SOME USEFUL PROTEIN.



FOR YOUR BACTERIAL DNA, YOU NEED SOMETHING THAT WILL BE REPLICATED ONCE IT'S RETURNED TO THE CELL — A "VECTOR," SO-CALLED



LUCKILY, *E. COLI* HAS SMALL RINGS OF DNA CALLED **PLASMIDS**, SEPARATE FROM THE CHROMOSOME. YOU CHOOSE (OR ENGINEER!) A PLASMID CONTAINING THE SEQUENCE G·A·A·T·T·C, AND REMOVE IT FROM THE BACTERIUM.

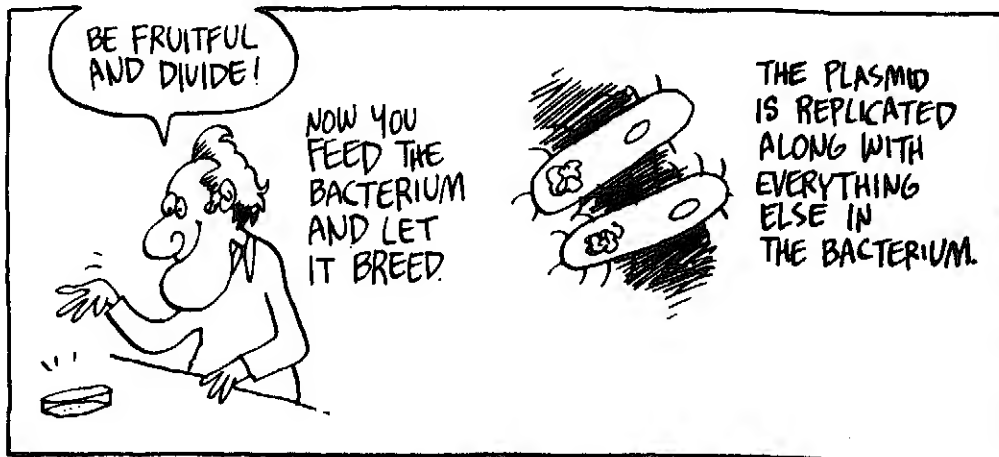


JUST AS ABOVE, YOU **SPLICE** THE HUMAN GENE INTO THE PLASMID —

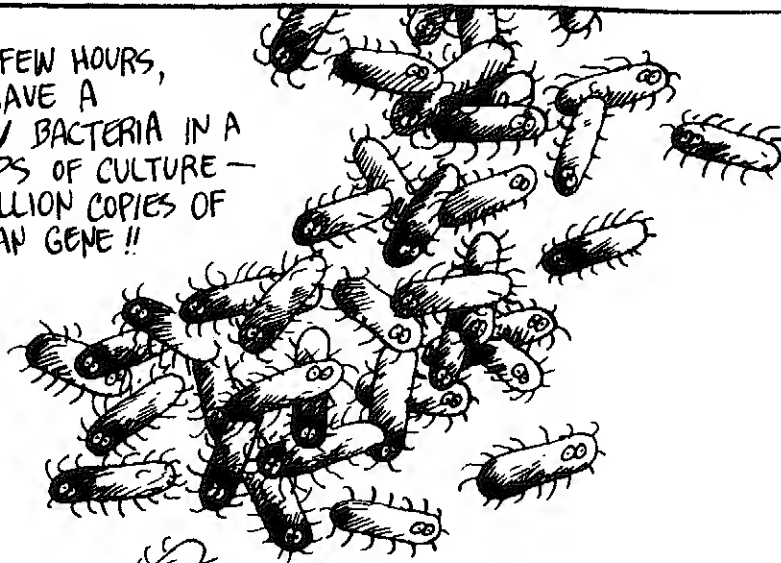


AND PUT IT BACK INTO *E. COLI*.





WITHIN A FEW HOURS,  
WE CAN HAVE A  
**BILLION** BACTERIA IN A  
FEW DROPS OF CULTURE —  
AND A BILLION COPIES OF  
THE HUMAN GENE !!



THE PROCEDURE SOUNDS SIMPLE — AND, IN PRINCIPLE, IT IS. IN PRACTICE IT CAN BE MOST COMPLICATED, BUT THE FOLKS IN THE LABS HAVE SOLVED MOST OF THOSE PRACTICAL PROBLEMS. WE CAN NOW CLONE JUST ABOUT ANY GENE WE WANT... USUALLY IN *E. COLI*, BUT OTHER FAST-GROWING ORGANISMS WORK, AS WELL, EVEN EUKARYOTES LIKE YEAST —



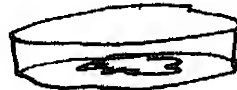
HI! NOT ONLY DO I FULFILL THE MINIMUM DAILY REQUIREMENT OF VITAMINS A, B, C, D, AND K, BUT ALSO I TASTE LIKE ROAST DUCKLING AND PREVENT CANCER!



'BREAD OF THE FUTURE!'

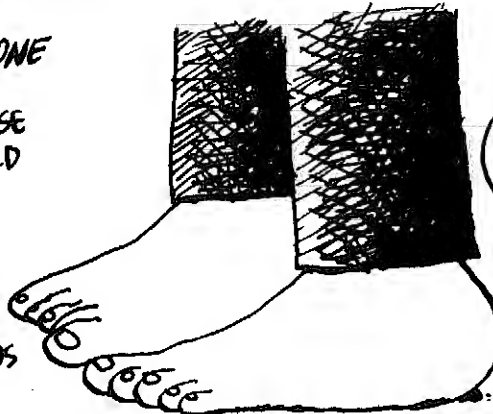
IT'S EVEN POSSIBLE TO CLONE GENES INTO HUMAN CELLS, BUT SO FAR IT ONLY WORKS IN A DISH, NOT IN A REAL PERSON...

BUT ONE OF THESE DAYS...



AT LEAST 3 PROTEINS NOW PRODUCED BY RECOMBINANT DNA HAVE MEDICAL POSSIBILITIES...

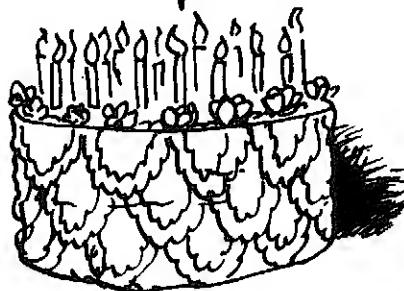
**HUMAN GROWTH HORMONE** PREVENTS ONE TYPE OF DWARFISM. PEOPLE WHOSE GENETIC MAKE-UP WOULD OTHERWISE LEAVE THEM A BIT "SHORT," CAN GROW NORMALLY IF GIVEN ADEQUATE DOSES. SO FAR, DEMAND STILL EXCEEDS SUPPLY, BUT NOT FOR "LONG"!



I THINK I G'D'D!

**INSULIN**, WHICH BREAKS DOWN SUGAR IN THE BLOOD, HAS LONG BEEN MADE BY OTHER MEANS... BUT SHOULD NOW BECOME MORE PLENTIFUL, AND POSSIBLY CHEAPER, MAKING LIFE EASIER FOR DIABETICS —

LET THEM EAT CAKE!



**INTERFERON**, THE VIRUS-FIGHTER, USED TO BE SO SCARCE IT COST A TRILLION DOLLARS AN OUNCE — BUT NOW IT'S MADE BY THE VASTFUL BY TRILLIONS OF *E. COLI*. UNFORTUNATELY, NO ONE KNOWS EXACTLY WHAT TO DO WITH IT, THOUGH CLINICAL TRIALS CONTINUE AMID HIGH HOPES...

IT MAY CURE CANCER OR THE COMMON COLD!





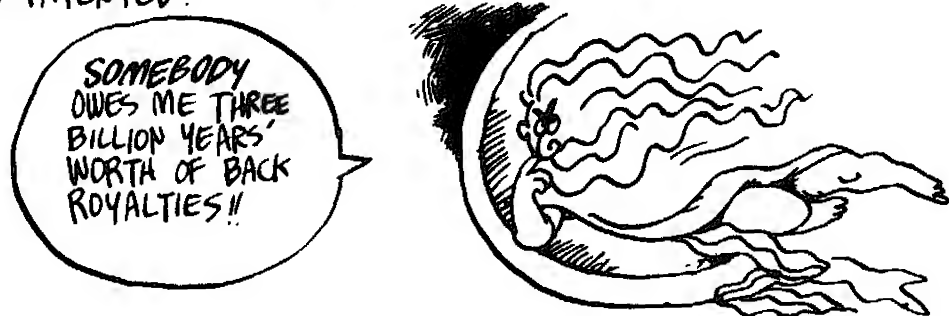
BACK IN THE UNIVERSITY, THIS IS THE CAUSE OF SOME CONCERN...







THIS QUESTION HAS ALREADY GONE TO THE SUPREME COURT, WHICH RULED THAT NEWLY INVENTED LIFE FORMS MAY BE PATENTED!



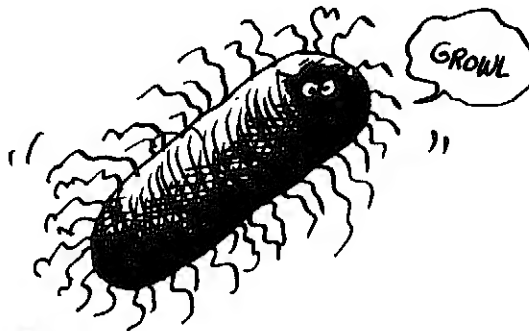


BUT FORGET ABOUT MONEY... WHAT ABOUT OUR **HEALTH** ?? FROM THE FIRST DAYS OF GENETIC ENGINEERING, PEOPLE HAVE WORRIED ABOUT BREEDING **MONSTERS** IN THE LAB !!

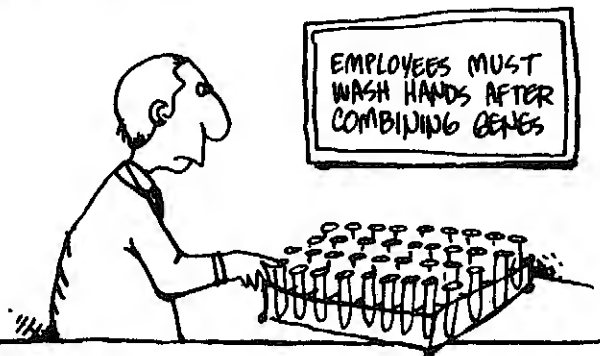


THE FEAR WAS THAT TAMPERING WITH E. COLI'S DNA MIGHT CREATE A SUPER-DEADLY GERM BY ACCIDENT.

REMEMBER, E. COLI LIVES IN THE HUMAN INTESTINE — IF A VIRULENT STRAIN SHOULD ESCAPE FROM THE LAB, THERE MIGHT BE NO STOPPING IT!! WHO'D HAVE THOUGHT FRANKENSTEIN'S MONSTER WOULD LOOK LIKE THIS?



ACCORDINGLY, SCIENTISTS VOLUNTARILY ADOPTED GUIDELINES TO LIMIT POTENTIAL HAZARDS...





THE MOST ENCOURAGING THING IS THIS: THE STRAIN OF E. COLI  
USUALLY USED FOR CLONING GENES HAS GROWN SO "DOMESTICATED"  
DURING ITS YEARS IN THE LAB, THAT IT CAN NO LONGER SURVIVE  
IN THE HUMAN GUT!!



**SO** MAYBE THERE'S NOTHING TO WORRY ABOUT...  
THOUGH IT'S TRUE THAT THE SAFEGUARDS  
ADOPTED BY UNIVERSITIES DON'T GENERALLY APPLY  
TO PRIVATE COMPANIES !!!

WHAT'S MUCH MORE LIKELY  
IS THAT SOMEONE WILL MAKE A  
DEADLY GERM ON PURPOSE.  
WHO WOULD WANT TO DO  
THAT, YOU ASK?

I CAN'T  
IMAGINE!!!



THE GENERALS HAVE BEEN KNOWN TO TURN NEW  
TECHNOLOGY TO MILITARY USE, AND  
THEY USUALLY FIND SCIENTISTS  
TO OBLIGE...

REPEAT AFTER  
ME: "IT'S PURE  
RESEARCH!"

IT'S... PURE...



WE CAN TAKE SOME COMFORT FROM THE FACT THAT BIOLOGICAL WARFARE IS BANNED BY INTERNATIONAL TREATY, BUT YOU NEVER KNOW...



LET ME TELL YOU ABOUT SOME BROKEN TREATIES!

IT'S A POLITICAL QUESTION RAISED BY A SCIENTIFIC ADVANCE—A FAMILIAR FACT OF 20<sup>TH</sup> CENTURY LIFE.

DOES THIS POTENTIAL FOR HARM MEAN THAT GENE SPLICING SHOULD BE STOPPED?? ALMOST WITHOUT EXCEPTION, THE BIOLOGISTS SAY "NO." WHY REJECT THE MEDICAL ADVANCES ALONG WITH THE MILITARY USES??

BESIDES, THE POISONS THAT COULD BE MADE THIS WAY ARE PROBABLY NO WORSE THAN THE ONES THAT ALREADY EXIST, WHILE MEDICAL ADVANCES PROMISE TO BE TRULY REVOLUTIONARY.



YEAH... LET US REALIZE OUR HUMAN POTENTIAL...



# ON THE VERGE



SO FAR, THE SUCCESSES IN THIS FIELD HAVE COME IN VIRUSES, BACTERIA, YEAST, AND PLANTS, BUT WE'RE GETTING MUCH CLOSER TO WORKING DIRECTLY WITH **HUMAN BEINGS**.

GAK!

HUMANS?

DISGUSTING!



WHEN MAKING TESTS ON HUMANS, SCIENTISTS MUST APPLY A **DIFFERENT STANDARD** FROM THAT GOVERNING EXPERIMENTS ON ANIMALS OR BACTERIA.

NAMELY, IT'S SUPPOSED TO DO THE SUBJECT SOME GOOD!



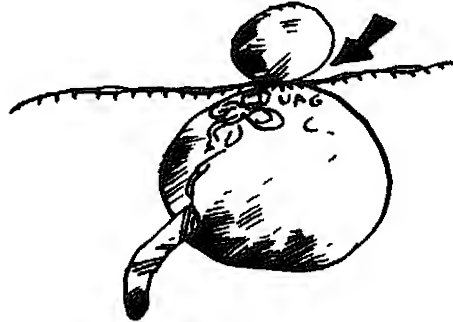
THAT'S WHY WE KNOW SO WELL WHAT CAUSES CANCER IN **RATS**... HOW COULD YOU DO AN EXPERIMENT TO FIND THE CAUSES OF CANCER IN **HUMANS??**

ASK FOR VOLUNTEERS?

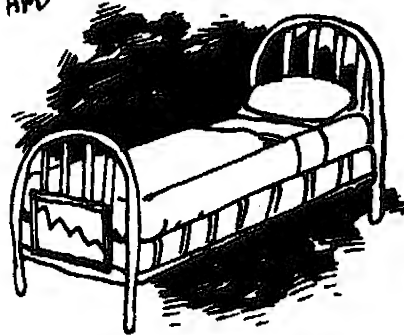


WHICH IS TO SAY, EXPERIMENTS ON HUMANS STIR UP CONTROVERSY, A GOOD EXAMPLE BEING RECENT ATTEMPTS TO TREAT THALASSEMIA.

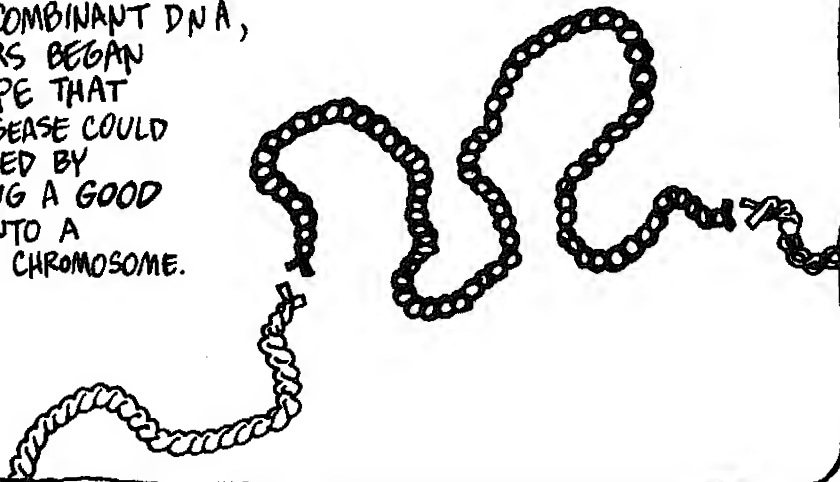
AS YOU RECALL, THIS CONDITION IS AN INABILITY TO MAKE HEMOGLOBIN, CAUSED BY A MISTAKEN "STOP" CODON IN THE MIDDLE OF THE GENE FOR ONE OF ITS CHAINS.

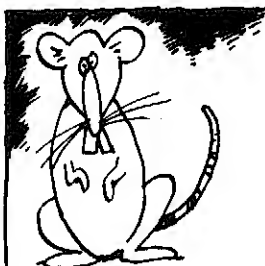


THALASSEMIA VICTIMS CAN SUFFER FROM ANEMIA, BONE DEFORMITIES, AND HEART PROBLEMS. THEY REQUIRE FREQUENT BLOOD TRANSFUSIONS TO SURVIVE, AND EVEN THEN THEY DON'T LIVE LONG.



WITH THE SUCCESS OF RECOMBINANT DNA, DOCTORS BEGAN TO HOPE THAT THE DISEASE COULD BE CURED BY SPLICING A GOOD GENE INTO A HUMAN CHROMOSOME.





SOUNDS GOOD, EXCEPT THAT THE SAME APPROACH HAD ALREADY FAILED REPEATEDLY IN MICE. STILL, A TEAM OF DOCTORS FROM U.C.L.A. DECIDED TO TRY IT ON HUMANS ANYWAY..!

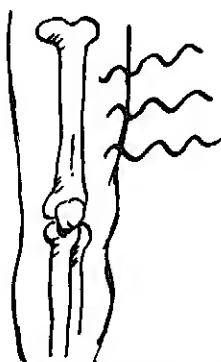


THEY REMOVED BONE MARROW CELLS FROM TWO PATIENTS' THIGH BONES. (REMEMBER, THESE DEVELOP INTO HEMOGLOBIN-PRODUCING RED BLOOD CELLS.)



A GOOD HEMOGLOBIN GENE WAS SPLICED IN.

THE THIGH WAS IRRADIATED TO SLOW DOWN THE OLD MARROW (AND GIVE THE NEW CELLS THE EDGE).



AND THE "ENGINEERED" CELLS WERE PUT BACK IN.



AND THE RESULT?

➡ ABSOLUTELY NOTHING!

(SINCE THEN, THE EXPERIMENT HAS WORKED — IN MICE.)



⚡SIGH⚡ THERE GOES THE EXPERIMENT...

AND THE PATIENT...

THE DOCTORS TOOK A LOT OF FLAK FOR THIS EXPERIMENT.



SEVERAL OBJECTIONS WERE RAISED:

NOT EVEN A PART OF THE PROCEDURE HAD EVER WORKED IN ANIMALS. IT'S STILL NOT AT ALL CLEAR HOW TO INSERT A HUMAN HEMOGLOBIN GENE INTO A MAMMAL CELL IN SUCH A WAY THAT IT'S EXPRESSED IN ANY QUANTITY.

REGULATION IN MAMMALS IS STILL MURKY!

THE EXPERIMENT WAS **DISAPPROVED** BY U.C.L.A.'S COMMITTEE ON HUMAN SUBJECTS USE. HOWEVER, IT HAD BEEN APPROVED BY THE TWO HOSPITALS WHERE IT WAS CARRIED OUT (IN ITALY AND ISRAEL).



THE RADIATION CERTAINLY DIDN'T HELP THE PATIENTS. ON THE OTHER HAND, THEY BOTH FULLY UNDERSTOOD WHAT WAS BEING DONE, AND THEY GAVE THEIR CONSENT.

WERE THEY GRASPING AT STRAWS?



AFTERWARDS, THE DOCTORS WERE DISCIPLINED, ONE OF THEM LOSING HIS POSITION AS DEPARTMENT CHAIRMAN... SO YOU SEE — HUMAN EXPERIMENTS CAN BE DANGEROUS!

DANGEROUS TO DOCTORS, THAT IS!





NEVERTHELESS, THIS IS PROBABLY THE WAY THE FIRST GENETIC THERAPIES WILL BE DONE, BECAUSE BONE MARROW IS THE EASIEST TISSUE TO TRANSPLANT.



THERE ARE SEVERAL DISEASES THAT MIGHT BE TREATED THIS WAY:

THALASSEMIA, OF COURSE, ALTHOUGH THE UCLA EXPERIENCE SHOWS IT WON'T BE EASY.



**SICKLE-CELL ANEMIA** IS A HEMOGLOBIN ABNORMALITY AFFECTING MAINLY BLACK PEOPLE. THIS WILL BE EVEN HARDER BECAUSE THE MUTANT GENE IS CODOMINANT, NOT RECESSIVE.



**HEMOPHILIA**, DUE TO THE LACK OF A BLOOD PROTEIN, MIGHT BE THE EASIEST TO CURE!



AND THERE ARE **IMMUNO-DEFICIENCY** DISEASES CAUSED BY RECESSIVE GENES IN BONE MARROW. AT PRESENT, PEOPLE WITH THESE DISEASES HAVE TO LIVE IN GERM-FREE ISOLATION CHAMBERS.



OF COURSE, THERE ARE FEWER RESTRICTIONS ON PLANT AND ANIMAL EXPERIMENTS THAN ON HUMANS. (THIS BOTHERS SOME PEOPLE, BY THE WAY.)



SO PROGRESS HAS BEEN MORE RAPID AMONG PLANTS AND ANIMALS. ALREADY THERE ARE BREEDS OF COTTON, TOMATO, AND TOBACCO WITH AN ADDED BACTERIAL GENE THAT MAKES THEM POISONOUS TO INSECTS.



SCIENTISTS ARE EXCITED ABOUT TRANSGENIC ANIMALS - ANIMALS THAT CONTAIN A FEW GENES FROM ANOTHER SPECIES.



ONE EXAMPLE ARE PIGS WITH BOVINE GROWTH HORMONE. THEY GROW FASTER AND LEANER, BUT ALSO HAVE OTHER PROBLEMS, LIKE ULCERS AND ARTHRITIS - SO YOU'LL HAVE TO WAIT FOR THAT "BORK" CHOP.



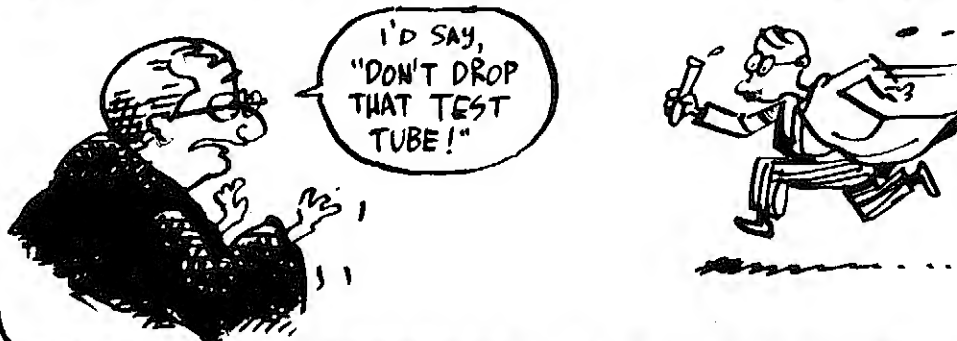
TRANSGENIC PLANTS AND ANIMALS CAN PASS ON THEIR NEW GENES TO THEIR OFFSPRING, BECAUSE THE GENES ARE INSERTED AT A VERY EARLY STAGE OF DEVELOPMENT, ALLOWING THEM TO GET INTO SPERM AND EGG CELLS. PERFORMING THESE EXPERIMENTS ON HUMANS WOULD THEREFORE RAISE SOME HARD ETHICAL ISSUES.



BUT WE'RE GETTING CLOSER. THERE ARE ALREADY LIVING "TEST TUBE BABIES" — FERTILIZED IN A TEST TUBE AND THEN, AFTER A FEW DIVISIONS, IMPLANTED IN THE MOTHER'S WOMB, WHERE THEY DEVELOPED NATURALLY.

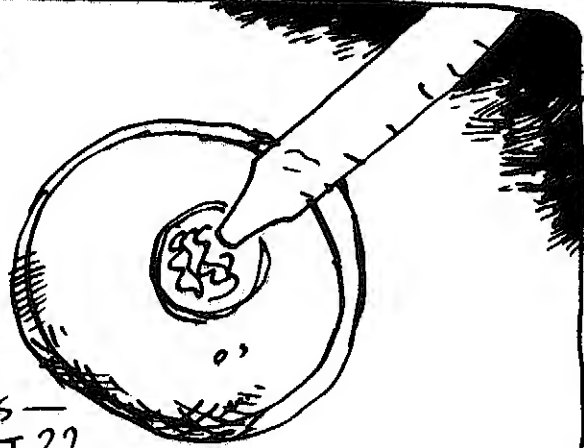


WHAT WOULD THE MONK MENDEL HAVE TO SAY ABOUT **THIS**?

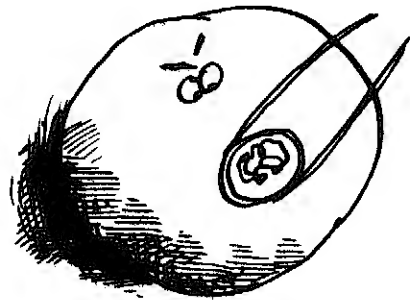
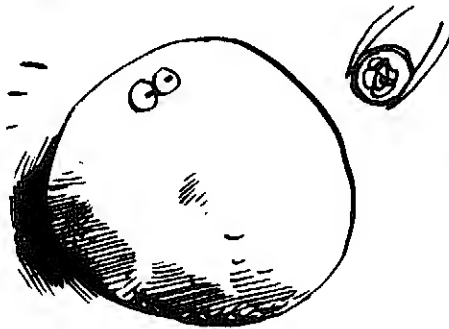


THE OBVIOUS NEXT STEP  
WOULD BE TO ENGINEER  
THE EMBRYO IN THE  
TEST TUBE...

THIS COULD RANGE FROM  
**GENE THERAPY** —  
FIXING SPECIFIC DEFECTS —  
TO... WHO KNOWS WHAT ??



AT THE EXTREME, IT MAY BECOME POSSIBLE TO CLONE  
PEOPLE. THE EGG'S NUCLEUS WOULD BE REMOVED  
ALTOGETHER AND REPLACED WITH A NUCLEUS FROM ANOTHER  
PERSON.



THIS EGG  
WOULD BE  
IMPLANTED  
IN A  
"MOTHER,"  
TO WHOM  
IT WOULD  
BE GENETICALLY  
UNRELATED.



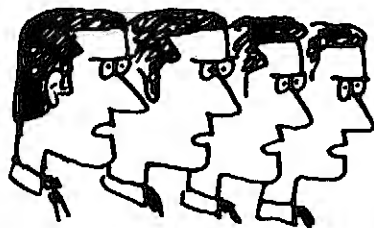
INSTEAD,  
THE LITTLE  
TYKE  
WOULD BE  
GENETICALLY  
IDENTICAL  
TO WHOEVER —  
OR WHATEVER —  
DONATED  
THE NUCLEUS.



SOUND FAR-FETCHED? WELL, SCIENTISTS HAVE ALREADY SUCCEEDED IN CLONING MICE AND FROGS...



THE TECHNIQUE MAKES IT POSSIBLE TO MAKE MULTIPLE COPIES OF LIVING INDIVIDUALS! IS THIS WHAT WE WANT TO BECOME, A WORLD OF CLONES??



WE SEE NOTHING WRONG WITH IT!

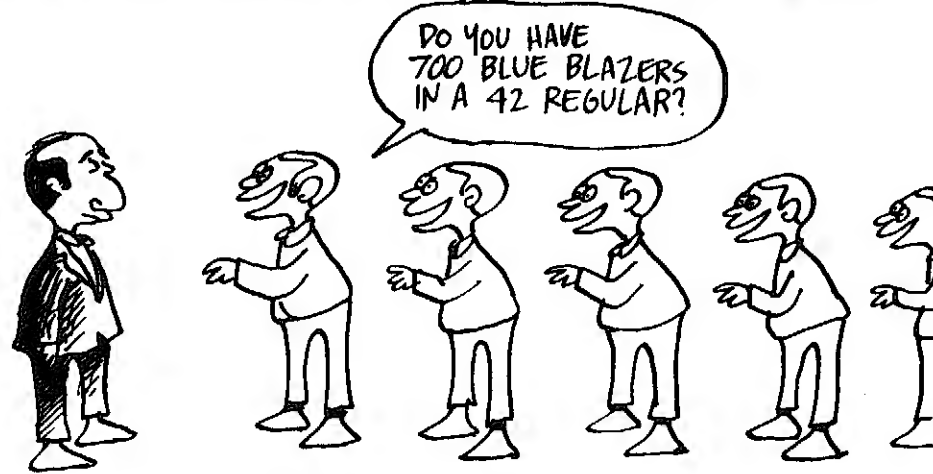
YOU MIGHT WELL ASK:  
WHO WILL BE CLONED?  
WHO WILL DECIDE? WILL  
IT BE BASED PURELY ON  
MONEY? WILL IT BE LEGAL?  
WILL THERE BE PEOPLE-  
BREEDERS SELECTING THE  
MOST "FIT" FOR REPRODUCTION?

STAND ASIDE,  
WEAKLINGS!



THE LAST TIME ANYONE  
TRIED TO BREED A MASTER  
RACE, IT WAS AN UNHAPPY  
EXPERIENCE, TO SAY THE LEAST...

OR MAYBE WE'RE BEING TOO GLOOMY... MAYBE THE FUTURE  
WILL BE A GLORIOUS TIME WHEN PEOPLE WILL BE  
ENGINEERED TO FIT CLOTHES INSTEAD OF VICE VERSA!!



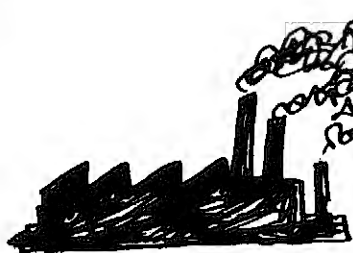
MAYBE  
WE CAN  
EVEN BE  
CLONED TO  
RESIST  
ECOLOGICAL  
DISASTER,  
LIKE THE  
DEPLETION  
OF  
ATMOSPHERIC  
OZONE!!



IT'S NOT ONLY OUR OWN GENES WE NEED TO WORRY ABOUT... THERE IS ALSO THE GENETIC DIVERSITY OF THE ENTIRE PLANET... (IT LOOKS SOMETHING LIKE A GIANT CELL, DOESN'T IT?)



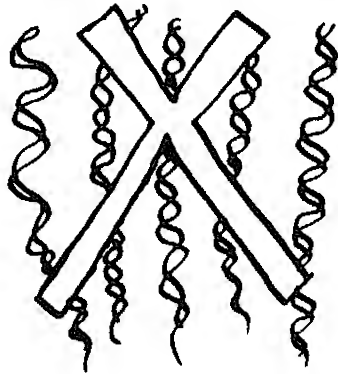
IT'S HARDLY NEWS THAT ALL LIFE IS INTERDEPENDENT... GORILLA EATS BANANA; BANANA EATS CHEMICALS FROM THE SOIL; SOME OF THE CHEMICALS GET THERE FROM BACTERIAL ACTION; OTHER BACTERIA AND THE APE'S DIGESTION; STILL OTHERS BREAK DOWN ITS WASTE PRODUCTS, ETC ETC ETC...



## BUT WE HUMANS

WITH OUR EXPLODING POPULATION, RESOURCE-HOGGING, MODERN AGRICULTURE, AND POLLUTION, ARE CHANGING THE ENVIRONMENT SO DRASTICALLY THAT HUNDREDS OF PLANT AND ANIMAL SPECIES GO EXTINCT EVERY YEAR.

THAT MEANS FEWER AND FEWER DIFFERENT GENES REMAIN IN THE BIOSPHERE. ONCE GONE, THEY'RE GONE FOREVER!



I DIDN'T MEAN TO DO IT!



THIS INCREASINGLY THREATENS LIFE AS A WHOLE...

FOR EXAMPLE, IF THERE ARE ONLY 5 KINDS OF APPLE, THEY MAY ALL BE WIPED OUT BY A VIRUS OR BLIGHT...

WHEREAS, IF THERE WERE 50 VARIETIES, CHANCES ARE BETTER THAT SOME OF THEM WILL BE RESISTANT AND SURVIVE.



HOW DO YOU LIKE THEM APPLES?



SEVERAL COUNTRIES ARE ADDRESSING THIS PROBLEM, SAVING AS MANY PLANTS AS POSSIBLE BY COLLECTING THEIR SEEDS.



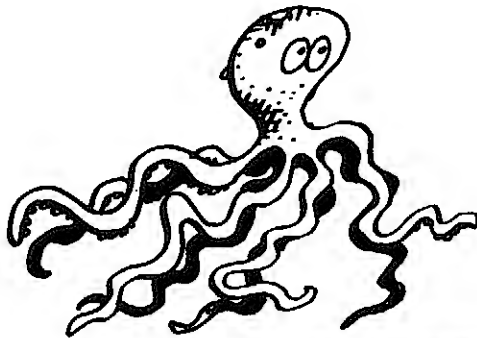
UNFORTUNATELY, THERE'S NO SUCH WAY TO SAVE ANIMALS.



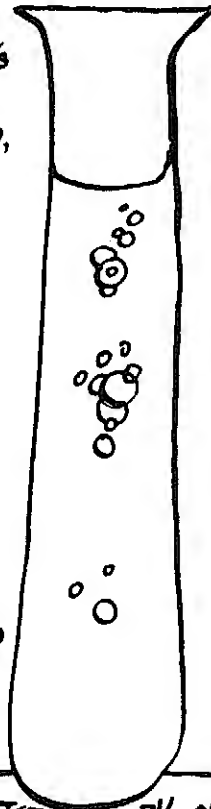


PERHAPS GENETIC ENGINEERING  
WILL BE ABLE TO HELP BY  
CREATING NEW COMBINATIONS,  
BUT THIS IS STILL IN THE  
FUTURE...

SAVE  
ME!!

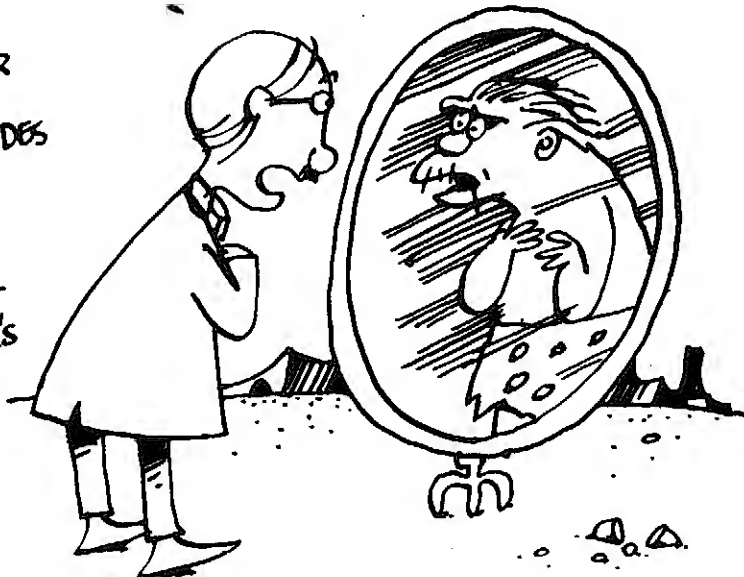


ON THE OTHER  
HAND, THE  
POSSIBILITIES  
FOR GENETIC  
ENGINEERING  
WILL BE  
LIMITED BY  
THE LIMITED  
NUMBER  
OF ALLELES  
LEFT TO  
RECOMBINE.

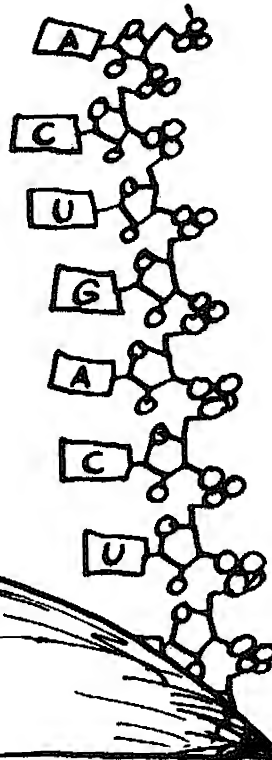


WE FIND OURSELVES CONFRONTED BY OUR OWN AWESOME  
POWERS.

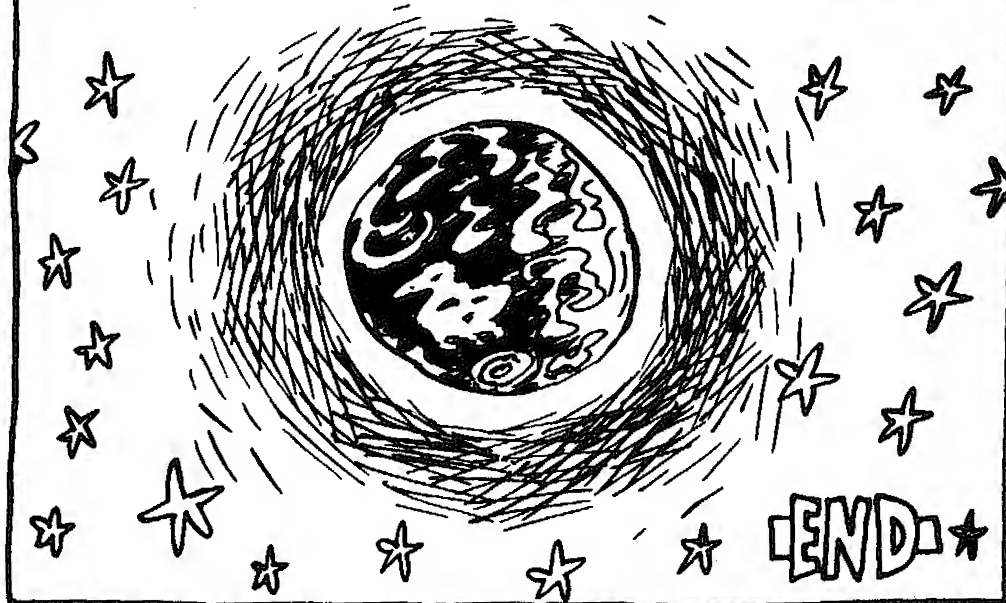
ON THE ONE  
HAND, WE  
FACE THE  
BLIND POWER  
THAT STRIPS  
FORESTS, ERODES  
THE SOIL,  
TURNS  
MARGINAL  
FARMLAND  
INTO DESERT,  
AND DEPLETES  
THE HEALTHY  
DIVERSITY  
OF THE  
GENE POOL...



ON THE OTHER HAND, WE MUST DEAL WITH THE GROWING POWER OF GENETIC ENGINEERING. IT PROMISES — OR THREATENS — TO ALTER THE VERY NATURE OF HUMANITY. IT RAISES QUESTIONS WHICH WE BARELY HAVE A VOCABULARY TO DISCUSS, MUCH LESS SOCIAL AND POLITICAL INSTITUTIONS TO DECIDE.



WITH POWER COMES THE RESPONSIBILITY OF CHOOSING WISELY. IN PART, THIS DEPENDS ON ACCURATE INFORMATION. IN A SENSE, WE HAVE COME FULL CIRCLE, TO A TIME WHEN EVERYONE MUST BE A BIOLOGIST, AND THE WORLD IS A CLASSROOM!



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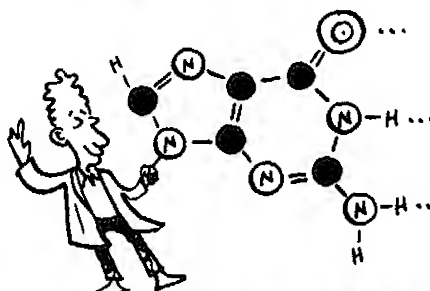
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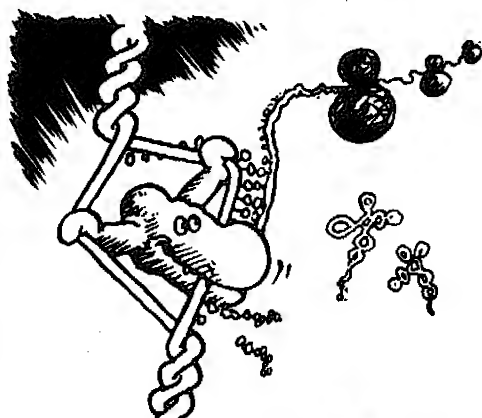


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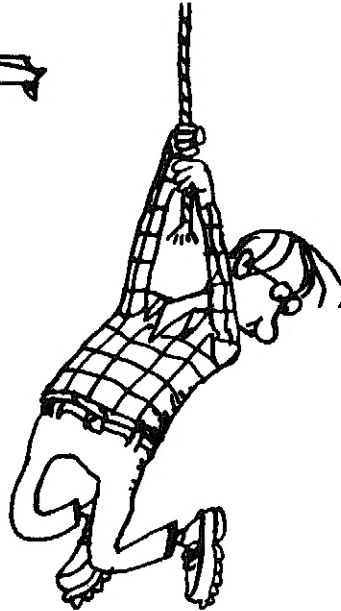
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Cover design and illustration © by Larry Gonick

**USA \$15.00**

**CANADA \$21.50**

ISBN 0-06-273099-1



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